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## IN ENGLISH TRANSLATION

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# CONTENTS

# CONTENTS (continued)

# CONTENTS (continued)

# CONTENTS (continued)

# SYNTHESIS OF HYDROCARBONS

## LXVI. $C_{11}$-$C_{16}$ HYDROCARBONS WITH TWO ADJACENT QUATERNARY CARBON ATOMS

R. Ia. Levina, P. A. Kaikaris, A. V. Simolin, and E. G. Treshchova

In our preceding communications [1,2] we described the reaction between alkyl magnesium bromides and tertiary bromides of the allyl type as a method of synthesis of alkenes containing one quaternary carbon atom (III and IV). The tertiary allyl bromides used were 2-bromo-2,4-dimethyl-3-pentene (Ia; hydrobromide of 2,4-dimethyl-1,3-pentadiene) [1] and 3-bromo-3,5-dimethyl-4-heptene (IIa, prepared by hydrobromination of a mixture of two isomeric dienic hydrocarbons with the same carbon skeleton but with different positions of one of the two double bonds —3,5-dimethyl-2,4-heptadiene and 3-methyl-5-ethyl-3,5-hexadiene) [2].

$$CH_3-C=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br + RMgBr \rightarrow CH_3-C=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-R$$

(Ia)                    (III)

$$C_2H_5-C=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{C_2H_5}{|}}{C}}-Br + RMgBr \rightarrow C_2H_5-C=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{C_2H_5}{|}}{C}}-R$$

(IIa)                    (IV)
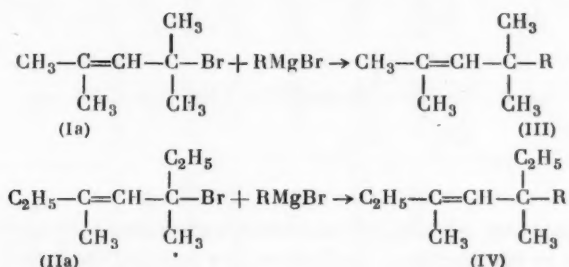
The yields of alkenes were 30%; the structure of some of them was confirmed by ozonization [1-3].

Subsequent investigation of this reaction showed that the yields of alkenes (III) can be raised to 50% by using a tertiary allyl chloride of structure (I) (hydrochloride of 2,4-dimethyl-1,3-pentadiene) in place of the corresponding bromide [3, 4].

In the present work we studied the reaction between tert-allyl chlorides $C_7H_{12}Cl$ and $C_9H_{17}Cl$ with structures (I) and (II) and organomagnesium compounds containing a tert-alkyl group as a method of synthesis of alkenes (V) and (VI) with two adjacent quaternary carbon atoms.

$$CH_3-C=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Cl + ClMg-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-R \rightarrow CH_3-C=CH-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-R \xrightarrow{+H_2}$$

(I)                        (V)

$$\rightarrow CH_3-CH-CH_2-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-R \text{ where } R = CH_3^\bullet,\ C_2H_5\ \&\ C_6H_{11}.$$

(VI)

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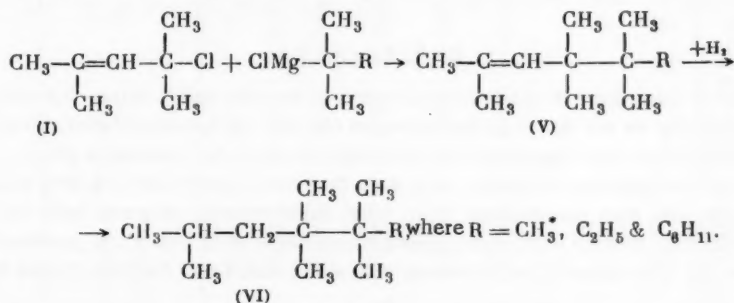
\* We previously synthesized [5] the alkenes and alkanes of structures (V), (VII) and (VI), (VIII), in which $R = CH_3$, from the corresponding tertiary allyl bromides (Ia and IIa).

$$
\begin{array}{c}
\underset{\substack{|\\CH_3}}{\overset{\substack{C_2H_5\\|}}{C_2H_5-C=CH-C-Cl}} + \underset{\substack{|\\CH_3}}{\overset{\substack{CH_3\\|}}{ClMg-C-R}} \rightarrow \underset{\substack{|\quad\;|\\CH_3\;CH_3}}{\overset{\substack{C_2H_5\;CH_3\\|\quad\;|}}{C_2H_5-C=CH-C-C-R}} \overset{+H_2}{\longrightarrow}
\end{array}
$$

(II)                                     (VII)

$$
\rightarrow \underset{\substack{|\qquad\quad|\quad\;|\\CH_3\qquad CH_3\;CH_3}}{\overset{\substack{C_2H_5\;CH_3\\|\quad\;|}}{C_2H_5-CH-CH_2-C-C-R}}, \text{where } R = CH_3,\; C_2H_5 \;\&\; C_3H_7
$$

(VIII)

Referring to the above equations, we see that the method was employed for synthesis of olefinic and paraffinic hydrocarbons of structures (V)-(VIII) containing 11-15 carbon atoms, as well as cyclohexanic hydrocarbons containing 16 carbon atoms with two quaternary carbon atoms in the side chain. The yields of unsaturated hydrocarbons (V) and (VII) were no more than 2-14% (calculated on the tert-alkyl magnesium chlorides whose content in the ethereal solution was determined by titration), due to secondary reactions involving facile cleavage of hydrogen chloride from the tertiary allyl chlorides (I) and (II) with formation of the original alkadienes $C_7H_{12}$ and $C_9H_{16}$ or their dimers, and also due to exchange reaction of these chlorides with the organomagnesium compounds so that after decomposition of the reaction mixture with water the alkenes (IX) $C_7H_{14}$ and $C_9H_{18}$ were formed [2, 5].

$$
\underset{\substack{|\quad\;|\\CH_3\;CH_3}}{\overset{\substack{R'\\|}}{R'-C=CH-C-Cl}} \overset{RC(CH_3)_2MgCl}{\longrightarrow} \underset{\substack{|\quad\;|\\CH_3\;CH_3}}{\overset{\substack{R'\\|}}{R'-C=CH-CMgCl}} \overset{H_2O}{\longrightarrow}
$$

$$
\rightarrow \underset{\substack{|\quad\;|\\CH_3\;CH_3}}{\overset{\substack{R'\\|}}{R'-C=CH-CH}}, \text{where } R' = CH_3 \;\text{(I)}\; \&\; C_2H_5 \;\text{(II)}.
$$

(IX)
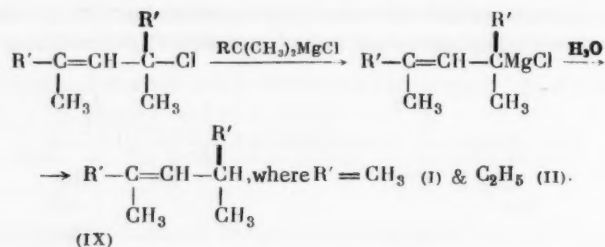
Olefinic hydrocarbons with two adjacent quaternary carbon atoms (V) and (VII) were isolated from the mixture of reaction products by two fractional distillations in a column. The Raman spectra of these hydrocarbons contained double-bond frequencies in the 1658-1668 cm$^{-1}$ region which confirmed their structure as trisubstituted olefins; the spectra of the corresponding alkanes contained strong lines in the 660-678, 930 and 1204-1240 cm$^{-1}$ regions, which are characteristic [6, 7] of complex branching (quaternary carbon atom) in a carbon chain.

Reactions between tertiary allyl chlorides and tert-alkyl magnesium chlorides can consequently serve as a method of synthesis of hydrocarbons with two adjacent quaternary carbon atoms. It should be noted that in the case of all of the alkenes that we synthesized (except the first one) and of the $C_{11}$-$C_{15}$ alkanes the molecular refractions (MR$_D$) found were very different (EM$_D$ from $-0.36$ to $-1.00$) from those calculated by the usual procedure (from the atomic refractions); at the same time the molar refractions of these hydrocarbons calculated by the additive procedure of V. M. Tatevskii [8], with allowance for the subtypes of chemical bond, are in good agreement with our experimental values (see Tables 1 and 2).

## EXPERIMENTAL

The tert-allyl chlorides — 2-chloro-2,4-dimethyl-3-heptene and 3-chloro-3,5-dimethyl-4-heptene — were obtained, respectively by the action of dry hydrogen chloride on 2,4-dimethyl-1,3-pentadiene [3, 4] and on a mixture of 3,5-dimethyl-2,4-heptadiene and 3-methyl-5-ethyl-3,5-hexadiene [2, 5]. The chlorides broke down on distillation of the hydrogen chloride; they were therefore brought into reaction with tert-alkyl magnesium chlorides immediately after their preparation. Tert-alkyl chlorides were prepared from the corresponding tert-alcohols by shaking for half an hour with concentrated hydrochloric acid which had previously been saturated with hydrogen chloride at 0°. The chlorides were washed with water, dried and distilled (yields 80-90%).

Tert-butyl chloride: b. p. 50° (736 mm), $n^{20}D$ 1.3859, $d_4^{20}$ 0.847. Tert-amyl chloride: b. p. 84-85° (744 mm), $n^{20}D$ 1.4047, $d_4^{20}$ 0.8623. 2-Chloro-2-methylpentane: b. p. 105-106° (740 mm), $n^{20}D$ 1.4125, $d_4^{20}$ 0.8605. 2-Chloro-2-cyclohexylpropane: b. p. 78° (12 mm), $n^{20}D$ 1.4708, $d_4^{20}$ 0.9626; MR$_D$ 46.62; calc. 46.43.

**TABLE 1**

Constants and Yields of $C_{11}$–$C_{16}$ Hydrocarbons of the Structure $R-C-C-C=C-R'$ (V and VII)

| General formula | R | R' | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | calculated allowing for sub-types of bond [8] | from atomic refractions | Frequency of double bond in Raman spectrum | Yield in g | in % calc. on organo-magnesium compound formed*** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $C_{11}H_{22}$* | $CH_3$ | $CH_3$ | 2,2,3,5-Penta-methyl-4-hexene | 172° (745) | 1.4470 | 0.7855 | 52.49 | 52.33 | 52.53 | 1664 | 52 | 14 |
| $C_{12}H_{24}$ | $C_2H_5$ | $CH_3$ | 3,3,4,6-Penta-methyl-5-heptene | 198.5—199 (750) | 1.4589 | 0.8099 | 56.79 | 56.72 | 57.15 | 1668 | 41 | 11 |
| $C_{13}H_{26}$** | $CH_3$ | $C_2H_5$ | 2,2,3,5-Tetra-methyl-3-ethyl-4-heptene | 71.5—72.5 (6) | 1.4552 | 0.8076 | 61.27 | 61.24 | 61.76 | 1660 | 31 | 13 |
| $C_{14}H_{28}$ | $C_2H_5$ | $C_2H_5$ | 3,3,4,6-Tetra-methyl-4-ethyl-5-octene | 97.5—98 (8) | 1.4620 | 0.8226 | 65.61 | 65.63 | 66.38 | 1658 | 41 | 10.5 |
| $C_{15}H_{30}$ | $C_3H_7$ | $C_2H_5$ | 4,4,5,7-Tetra-methyl-5-ethyl-6-nonene | 238—239 (760) | 1.4690 | 0.8345 | 70.21 | 70.26 | 71.00 | — | 11 | 2 |
| $C_{16}H_{30}$ | $C_6H_{11}$ | $CH_3$ | 2,3,3,5-Tetra-methyl-2-cyclo-hexyl-4-hexene | 125—127 (4) | 1.4916 | 0.8836 | 72.98 | — | 73.42 | — | 13 | 10 |

* Literature data: b. p. 170–170.2° (760 mm), $n^{20}D 1.4470$, $d_4^{20}$ 0.7836, $MR_D$ 52.60 [5]; b. p. 175° (760 mm), $n^{20}D$ 1.4461 (isolated from the mixture of hydrocarbons formed on dimerization of triptene with sulfuric acid [9].

** Literature data [5]: b. p. 210.5–211° (755 mm), $n^{20}D$ 1.4574, $d_4^{20}$ 0.8012, $MR_D$ 61.91.

*** Yields of organomagnesium compounds from tert-$C_4H_9Cl$, tert-$C_5H_{11}Cl$, tert-$C_6H_{13}Cl$, and 2-chloro-2-cyclohexylpropane were, respectively, 70, 60, 65 and 30%.

## TABLE 2

Constants of $C_{11}$–$C_{16}$ Hydrocarbons of Structure R—C—C—C—C—R′ (VIandVIII)

$$\begin{array}{c} \quad\ \text{C}\ \ \text{R}' \\ \text{R—C—C—C—C—C—R}' \\ \quad\ \text{C}\ \ \text{C} \end{array}$$
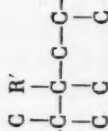
| General formula | R′ | R | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calculated allowing for sub. types of bond[8] | $MR_D$ calculated from atomic refractions[8] | Strong frequencies in the Raman spectra characteristic of complex chain branching (cm$^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|---|
| $C_{11}H_{24}$ * | $CH_3$ | $CH_3$ | 2,2,3,3,5-Pentamethylhexane | 170° (721) | 1.4296 | 0.7673 | 52.60 | 52.55 | 52.99 | 678, 926, 1240 |
| $C_{12}H_{26}$ | $C_2H_5$ | $CH_3$ | 3,3,4,4,6-Pentamethylheptane | 189 (730) | 1.4402 | 0.7892 | 56.92 | 56.94 | 57.62 | 675, 930, 1207 |
| $C_{13}H_{28}$ ** | $CH_3$ | $C_2H_5$ | 2,2,3,5,6-Tetramethyl-3-ethylheptane | 214—214.2(725) | 1.4470 | 0.8013 | 61.45 | 61.42 | 62.23 | 660, 929, 1219 |
| $C_{14}H_{30}$ | $C_2H_5$ | $C_2H_5$ | 3,3,4,6-Tetramethyl-4-ethyloctane | 108.5—109 (9) | 1.4540 | 0.8156 | 65.85 | 65.82 | 66.85 | 663, 912, 930, 1204, 1219 |
| $C_{15}H_{32}$ | $C_3H_7$ | $C_2H_5$ | 4,4,5,7-Tetramethyl-5-ethylnonane | 122—123(28) | 1.4590 | 0.8197 | 70.49 | 70.47 | — | — |
| $C_{16}H_{32}$ | $C_6H_{11}$ | $CH_3$ | 2,3,3,5-Tetramethyl-2-cyclohexylhexane | 135—136(5) | 1.4679 | 0.8464 | 73.67 | — | 73.88 | 753, 930, 1196 |

* Literature data [5]: b. p. 172.8–173.5° (760 mm), $n^{20}D$ 1.4302, $d_4^{20}$ 0.7673, $MR_D$ 52.88.

** Literature data [5]: b. p. 214–215° (750 mm), $n^{20}D$ 1.4442, $d_4^{20}$ 0.7934, $MR_D$ 61.80.

## TABLE 3

Analytical Results

| General formula | | $C_{12}H_{24}$ | $C_{12}H_{26}$ | $C_{14}H_{30}$ | $C_{11}H_{30}$ | $C_{14}H_{30}$ | $C_{15}H_{32}$ | $C_{16}H_{30}$ | $C_{16}H_{33}$ |
|---|---|---|---|---|---|---|---|---|---|
| C | Found % | 85.64, 85.81 | 84.69, 84.86 | 85.68, 85.84 | 84.57, 84.72 | 85.62, 85.77 | 84.86, 84.69 | 86.45, 86.32 | 85.64, 85.80 |
| | Calculated % | 85.63 | 84.62 | 85.62 | 84.76 | 85.63 | 84.76 | 86.41 | 85.63 |
| H | Found % | 14.32, 14.36 | 15.36, 15.10 | 14.34, 14.37 | 15.37, 15.18 | 14.36, 14.42 | 15.10, 14.98 | 13.64, 13.36 | 14.31, 14.39 |
| | Calculated % | 14.37 | 15.38 | 14.37 | 15.24 | 14.37 | 15.18 | 13.59 | 14.37 |

<u>Reaction of tert-allyl chlorides with tert-alkyl magnesium chlorides.</u> Into an ethereal solution of the organomagnesium compound prepared by slow addition of 2.2 moles tert-alkyl chloride in 800 ml of absolute ether to 2 atoms magnesium (activated with a few drops of methyl iodide) in 350 ml ether, was gradually stirred (cooling to $-40°$) a 1 : 1 ethereal solution of freshly distilled tert-allyl chloride — 2-chloro-2,4-dimethyl-3-heptene or 3-chloro-3,5-dimethyl-4-heptene — in quantity equimolar with the organomagnesium compound formed (the content of the latter in the ethereal solution was determined in a separate sample by titration — see Table 1). The reaction mixture was stirred for 2 hrs with the same degree of cooling, then for 2 hrs at room temperature, and for several hours with heating. After the reaction mixture had been decomposed (by pouring onto ice containing 10% hydrochloric acid or ammonium chloride), the ethereal extracts were worked up in the usual manner, the ether and the low-boiling fractions (up to 100°) were distilled off, and the residue was boiled with sodium (until the reaction for halogen was negative). The product was distilled off from polymers in vacuo and finally distilled over sodium in a column. Each experiment was carried out twice. Constants and yields of olefinic hydrocarbons with two adjacent quaternary carbon atoms (V and VII), isolated after two distillations in a column,* are presented in Table 1; the analytical results appear in Table 3.

The olefinic hydrocarbons were hydrogenated over nickel on alumina at 170-180°. The catalyzates (which did not decolorize bromine water) were washed with 80% sulfuric acid, with water, and with sodium carbonate until neutral, and distilled over sodium in a column. The constants of the resulting paraffinic hydrocarbons with two adjacent quaternary carbon atoms (VI and VIII) are presented in Table 2, while analytical results appear in Table 3.

## SUMMARY

1. Reaction of tert-allyl chlorides with tert-alkyl magnesium chlorides was used as a method of synthesis of olefinic hydrocarbons containing two adjacent quaternary carbon atoms.

2. $C_{11}$-$C_{16}$ hydrocarbons of the structure in question were synthesized by this method from 2-chloro-2,4-dimethyl-3-pentene (hydrochloride of 2,4-dimethyl-1,3-pentadiene) and 3-chloro-3,5-dimethyl-4-heptene (obtained by hydrochlorination of a mixture of isomeric dienes with the same carbon skeleton but with different positions of one double bond — 3,5-di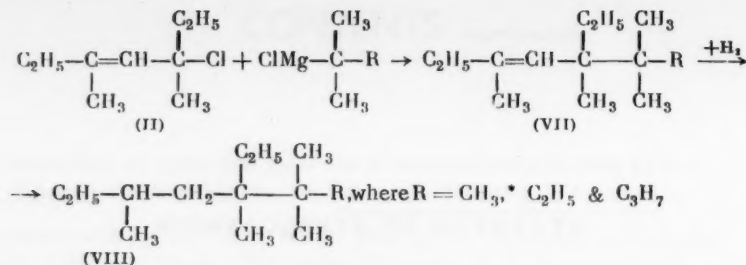methyl-2,4-heptadiene and 3-methyl-5-ethyl-3,5-hexadiene): 2,2,3,3,5-pentamethyl-4-hexene; 2,2,3,5-tetramethyl-3-ethyl-4-heptene; 3,3,4,4,6-pentamethyl-5-heptene; 3,3,4,6-tetramethyl-4-ethyl-5-octene; 4,4,5,7-tetramethyl-5-ethyl-6-nonene; also 2,3,3,5-tetramethyl-2-cyclohexyl-4-hexene. The last four compounds are here described for the first time.

3. Hydrogenation of these olefinic hydrocarbons led to the corresponding paraffinic hydrocarbons with two adjacent quaternary carbon atoms: 2,2,3,3,5-pentamethylhexane; 2,2,3,5-tetramethyl-3-ethylheptane; 3,3,4,4,6-pentamethylheptane; 3,3,4,6-tetramethyl-4-ethyloctane; 4,4,5,7-tetramethyl-5-ethylnonane; also 2,3,3,5-tetramethyl-2-cyclohexylhexane. The last four compounds have not previously been described.

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[6] B. I. Stepanov, J. Phys. Chem. 20, 917 (1946).

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* In all of the reactions carried out with 2-chloro-2,4-dimethyl-3-pentene (I), distillation gave a fraction consisting of the dimer of 2,4-dimethyl-1,3-pentadiene (b. p. 218-219° at 750 mm; 90° at 10 mm, $n^{20}D$ 1.4800) [1]; the reactions with 3-chloro-3,5-dimethyl-4-heptene (II) gave a fraction whose constants identified it as 3,5-dimethyl-3-heptene (IX, R' = $C_2H_5$; b. p. 130.5-131° at 750 mm, $n^{20}D$ 14220) [2].

** Original Russian pagination. See C. B. translation.

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# REACTION OF TERT–BUTYLBENZENE β-(MAGNESIUM CHLORIDE)
## WITH CARBONYL COMPOUNDS

A. D. Petrov, G. I. Nikishin, V. N. Gramenitskaia, and V. D. Vorob'ev

1-Chloro-2-methyl-2-phenylpropane ($C_6H_5$—$C(CH_3)_2$—$CH_2Cl$) is easily synthesized by chloroalkylation of benzene with methallyl chloride [1]. No studies have previously been made, however, of the possibilities of utilization of this halide — a structural analog of neopentyl chloride — in organomagnesium synthesis. The present investigation was undertaken with the aim of finding reliable methods of synthesis of alkylbenzenes containing a long branched chain with a quaternary carbon at the ring. As we know, such hydrocarbons were until recently obtained mainly by alkylation of benzene with tertiary alcohols in presence of $AlCl_3$. This method did not always ensure preparation of the pure forms [2]. Condensation of the Grignard reagent from the above halide with aldehydes gives secondary alcohols in high yield (53.5-72.5%). The properties of these alcohols are presented in the table. The yields of tertiary alcohols obtained by reaction of tert. butylbenzene β-(magnesium chloride) with ketones (acetone and methyl ethyl ketone) were very much lower (22 and 37%). This is evidently due to the circumstance that part of the ketone is reduced to secondary alcohol. These ketones are similarly reduced under the action of isobutyl magnesium chloride, as previously established [3].

In the case of methyl formate the main product was a secondary alcohol — 2,6-dimethyl-2,6-diphenyl-4-heptanol — i. e., a compound formed according to the normal mechanism

$$2C_6H_5-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2MgCl + H-C\overset{O}{\underset{OCH_3}{\diagdown}} \longrightarrow \left( C_6H_5-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2 \right)_2 CHOH$$
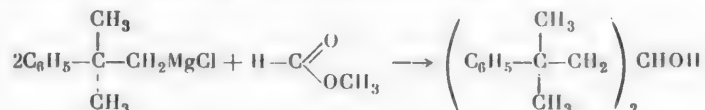
This alcohol or its formic ester was obtained in yields dependent on the conditions of synthesis and ranging between 45 and 68%. Reduction reactions also occur here, as evidenced by the formation of the formic acid ester and a primary alcohol — 3-methyl-3-phenyl-1-butanol (resulting from reduction of the aldehyde).

$$C_6H_5-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2MgCl + H-C\overset{O}{\underset{OCH_3}{\diagdown}} \rightarrow C_6H_5-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2-C\overset{O}{\underset{H}{\diagdown}} \rightarrow$$

$$\rightarrow C_6H_5-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2-CH_2-O-C\overset{O}{\underset{H}{\diagdown}}$$
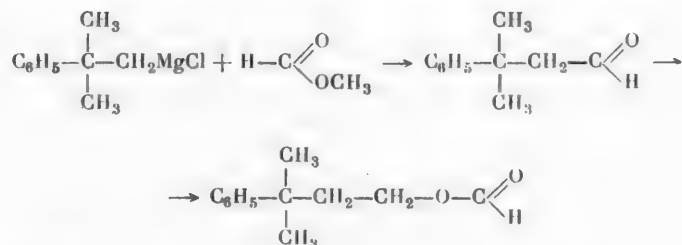
Formic esters of alcohols are products of their transesterification with methyl formate. The reaction of tert-butylbenzene β-(magnesium chloride) with ethyl acetate only went to the stage of formation of ketone (but not of tertiary alcohol), the ketone being reduced to secondary alcohol which was esterified by the ethyl acetate.
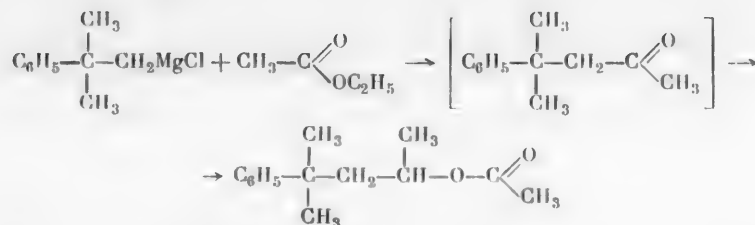
The ketone was evidently reduced by addition of 2MgCl at the carbonyl group, as evidenced by secondary formation of the hydrocarbon 2,5-dimethyl-2,5-diphenylhexane $C_6H_5C(CH_3)_2CH_2CH_2C(CH_3)_2C_6H_6$. The reaction with trimethylacetyl chloride evidently went in similar fashion. Here, however, the ester of the secondary alcohol was accompanied by the free alcohol 2,5,5-trimethyl-2-phenyl-4-hexanol (VI). This alcohol could be prepared in the pure form by reaction of tert-butyl magnesium chloride with β-phenylisovaleryl chloride.

## EXPERIMENTAL

Reaction of tert-butylbenzene β-(magnesium chloride) with aldehydes and ketones. The reaction was performed under standard conditions with the same ratios of components in all of the experiments. An excess of carbonyl compound was taken. We give details of a typical experiment. In the course of 4 hrs 200 g β-chloro-tert-butylbenzene was added, after reaction had commenced, to 48.6 g magnesium in 500 ml ether. After completion of the addition, the mass was stirred for 1 hr. Addition was then made of 130 g isovaleraldehyde and stirring was continued for another 12 hrs. After the reaction mass had been decomposed with water and weak hydrochloric acid, 168 g (61%) 2,7-dimethyl-2-phenyl-4-heptanol was isolated from the ethereal solution. In other experiments tert-butylbenzene β-(magnesium chloride) was reacted with acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, acetone and methyl ethyl ketone. The properties of the synthesized alcohols — 2-methyl-2-phenyl-4-pentanol (I), 2-methyl-2-phenyl-4-hexanol (II), 2-methyl-2-phenyl-4-heptanol (III), 2,5-dimethyl-2-phenyl-4-hexanol (IV), 2,7-dimethyl-2-phenyl-4-heptanol (V), 2,5-dimethyl-2-phenyl-4-pentanol (VII) and 2,5-dimethyl-2-phenyl-4-hexanol (VIII) — and their yields are presented in the table.

Preparation of 2-methyl-2-phenyl-4-bromoheptane. Hydrogen bromide was bubbled at 100° for 16 hrs through a layer of alcohol (III) (87.5 g). The reaction mass was then washed with 90% sulfuric acid and water, dried, and distilled to give 70 g 2-methyl-2-phenyl-4-bromoheptane (XV). Attempts to replace the hydroxyl by bromine with the help of phosphorus tribromide and 40% hydrobromic acid were unsuccessful.

Reaction of tert-butylbenzene β-(magnesium chloride) with esters. 1) Reaction with methyl formate. A. 180 g methyl formate diluted with twice as much ether was added with continuous stirring to tert-butylbenzene β-(magnesium chloride), prepared from 253 g β-chloro-tert-butylbenzene and 60 g Mg, at 5° in the course of 2 hrs. Considerable heat was developed during the reaction. The following substances were separated by fractional distillation:

Tert-butylbenzene: 30 g (14.8%), b. p. 82-85° (50 mm), $n^{20}D$ 1.4930; literature data [1]: b. p. 84.2° (50 mm), $n^{20}D$ 1.4924.

Formic ester of 2-methyl-2-phenyl-1-butanol (X): 21 g (7.3%). Its saponification with 5% alcoholic and 10% aqueous NaOH solution does not go to completion, as evidenced by the ester number (found 265.95; calculated 291.8), analyses for active hydrogen (0.818), and the elemental analysis of the alcohol obtained by saponification. Found %: C 79.15, 79.36; H 9.47, 9.43. $C_{11}H_{16}O$. Calculated %: C 80.44; H 9.82.

Formic ester of 2,6-dimethyl-2,6-diphenyl-4-heptanol (XII): 164 g (68%). Its saponification with 10% alcoholic solutions of NaOH and KOH did not go to completion even after prolonged boiling, as indicated by its ester number (found 163.3, calculated 172.9), and by the properties of the substance (b. p. 174°, at 1 mm, $n^{20}D$ 1.5420, $d_4^{20}$ 1.0100) obtained by saponification, which did not correspond either to those of the original ester or of alcohol (IX) (see table). The ester is not saponified at all by 10% aqueous NaOH.

B. Instead of the ethereal solution of methyl formate being added to the Grignard reagent, the reverse procedure was followed. The same quantities of starting components were taken and the Grignard reagent was

| Substance No. | Structure and name of compound | Yield (%) | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ calc. from refractions of atoms | $MR_D$ calc. from refractions of bonds | $MR_D$ found | Analysis found (%) C | Analysis found (%) H | empirical formula | calculated (%) C | calculated (%) H |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (I) | $C_6H_5C(CH_3)_2CH_2CHOHCH_3$ <br> 2-Methyl-2-phenyl-4-pentanol | 72.5 | 148—149° (13) | 1.5130 | 0.9697 | 55.54 | 55.87 | 55.25 | — | — | — | — | — |
| (II) | $C_6H_5C(CH_3)_2CH_2CHOHC_2H_5$ <br> 2-Methyl-2-phenyl-4-hexanol | 72.7 | 112—113 (4) | 1.5100 | 0.9592 | 60.15 | 60.51 | 59.95 | 81.07, 81.08 | 10.56,10.63 | $C_{13}H_{20}$ | 81.19 | 10.48 |
| (III) | $C_6H_5C(CH_3)_2CH_2CHOHC_3H_7$ <br> 2-Methyl-2-phenyl-4-heptanol | 53.5 | 128 (2) | 1.5030 | 0.9470 | 64.78 | 65.16 | 64.51 | 80.90, 80.97 | 10.23,10.07 | $C_{14}H_{22}O$ | 81.48 | 10.76 |
| (IV) | $C_6H_5C(CH_3)_2CH_2CHOHCH(CH_3)_2$ <br> 2,5-Dimethyl-2-phenyl-4-hexanol | 56.0 | 95.5 (2.5) | 1.5072 | 0.9516 | 64.78 | 65.16 | 64.65 | 81.00, 80.92 | 10.67,10.68 | $C_{14}H_{22}O$ | 81.48 | 10.76 |
| (V) | $C_6H_5C(CH_3)_2CH_2CHOHCH(CH_3)_2$ <br> 2,7-Dimethyl-2-phenyl-4-heptanol | 61.0 | 117 (2) | 1.5021 | 0.9366 | 69.39 | 69.83 | 69.43 | 82.01, 81.87 | 10.99,11.01 | $C_{15}H_{24}O$ | 81.75 | 10.49 |
| (VI) | $C_6H_5C(CH_3)_2CH_2CHOHC(CH_3)_3$ <br> 2,5,5-Trimethyl-2-phenyl-4-hexanol | 58.5 | 113—114 (3)* | — | — | — | — | — | 81.44, 81.43 | 10.86,10.80 | $C_{15}H_{24}O$ | 81.75 | 10.49 |
| (VII) | $C_6H_5C(CH_3)_2CH_2C(CH_3)_2OH$ <br> 2,5-Dimethyl-2-phenyl-4-pentanol | 22.6 | 108.5—109 (4) | 1.5130 | 0.9629 | 60.15 | 60.51 | 60.02 | 80.42, 80.38 | 10.60,10.46 | $C_{13}H_{20}O$ | 81.19 | 10.48 |
| (VIII) | $C_6H_5C(CH_3)_2CH_2C(CH_3)(OH)C_2H_5$ <br> 2,5-Dimethyl-2-phenyl-4-hexanol | 37.0 | 101—101.5 (1.5) | 1.5094 | 0.9565 | 64.78 | 65.16 | 64.44 | — | — | — | — | — |
| (IX) | $C_6H_5C(CH_3)_2CH_2CHOHCH_2C(CH_3)_2C_6H_5$ <br> 2,6-Dimethyl-2,6-diphenyl-4-heptanol | 55.0 | 167—168 (1) | 1.5428 | 1.008 | 93.50 | 94.21 | 93.41 | 84.46, 84.71 | 9.51, 9.50 | $C_{21}H_{28}O$ | 85.08 | 9.52 |
| (X) | $C_6H_5C(CH_3)_2CH_2CH_2CH_2OOCH$ <br> Formic ester of 2-methyl-2-phenyl-1-butanol | 7.3 | 81 (2) | 1.5070 | 1.0204 | 55.67 | 56.05 | 56.07 | 74.85, 74.75 | 8.24, 8.21 | $C_{12}H_{16}O_2$ | 74.96 | 8.38 |
| (XI) | $C_6H_5C(CH_3)_2CH_2CH(CH_3)OCOCH_3$ <br> Acetic ester of 2-methyl-2-phenyl-4-pentanol | 17.6 | 101—102 (3) | 1.4980 | 0.9966 | 64.80 | 65.39 | 64.78 | 76.53, 76.47 | 8.71, 8.79 | $C_{14}H_{20}O_2$ | 76.32 | 9.15 |
| (XII) | $C_6H_5C(CH_3)_2CH_2CH(OOCH)CH_2C(CH_3)_2C_6H_5$ <br> Formic ester of 2,6-dimethyl-2,6-diphenyl-4-heptanol | 68.0 | 174.5 (2) | 1.5350 | 1.0279 | 98.25 | 99.08 | 98.27 | 81.68, 81.69 | 8.73, 8.72 | $C_{22}H_{28}O_2$ | 81.44 | 8.7 |
| (XIII) | $C_6H_5C(CH_3)_2CH_2CH=CHC(CH_3)_2C_6H_5$ <br> 2,6-Dimethyl-2,6-diphenyl-4-heptene | 94.5 | 140—141° (2) | 1.5445 | 0.9578 | 91.51 | 92.21 | 91.65 | 90.35, 90.63 | 9.55, 9.55 | $C_{21}H_{26}$ | 90.58 | 9.42 |
| (XIV) | $C_6H_5C(CH_3)_2CH_2COCl$ <br> β-Phenylisovaleryl chloride | 94.0 | 97 (2) | 1.5220 | 1.1023 | 54.64 | 54.49 | 54.42 | — | — | — | — | — |
| (XV) | $C_6H_5C(CH_3)_2CH_2CHBrC_3H_7$ <br> 2-Methyl-2-phenyl-4-bromoheptane | 61.0 | 121—125 (2) | 1.5170 | 1.1455 | 71.02 | 71.35 | 70.99 | 62.60, 62.68 | 8.09, 8.01 | $C_{14}H_{21}Br$ | 62.44 | 7.86 |

* M. p. 45.5°.

introduced in the course of an hour, after which the reaction mixture was stirred for another 6 hrs at the boiling point of ether. The reaction gave 21% tert-butylbenzene, 21% of the formic ester of 2-methyl-2-phenyl-1-butanol (X) and 49.2% of the formic ester of 2,6-dimethyl-2,6-diphenyl-4-heptanol (XII).

C. 38 g of methyl formate, diluted with double the quantity of ether, was run into the tert-butylbenzene $\beta$-(magnesium chloride) prepared from 316 g $\beta$-chloro-tert-butylbenzene and 60 g Mg at the boiling point of ether. The reaction mixture was then stirred for another 1 hr. Fractional distillation gave the following substances:

Tert-butylbenzene: 52.5 g (23.3%), b. p. 85-87° (53 mm), $n^{20}D$ 1.4924; and 2,6-dimethyl-2,6-diphenyl-4-heptanol (IX): 103 g (55%).

Dehydration of 2,6-dimethyl-2,6-diphenyl-4-heptanol. 25 g of the alcohol was heated for an hour at 100° with 8 g oxalic acid. Fractional distillation gave 22 g (94%) of 2,6-dimethyl-2,6-diphenyl-4-heptene (XIII).

2) Reaction with ethyl acetate was performed under the same conditions as with methyl formate, using 260 g $\beta$-chloro-tert-butylbenzene, 50 g Mg and 264 g ethyl acetate. The Grignard reagent was run into the ethereal solution of ethyl acetate. Considerable heat was developed. Fractional distillation of the reaction products gave the following:

Tert-butylbenzene: 114 g (59%), b. p. 89-90° (60 mm), $n^{20}D$ 1.4910; acetic ester of 2-methyl-2-phenyl-4-pentanol (XI): 29 g (17.6%); 2,5-dimethyl-2,5-diphenylhexane: 37 g (20.5%), b. p. 157-158° (3 mm), m. p. 59.5-60°. Literature [4]: m. p. 60-61°. Found %: C 89.95, 89.97; H 10.01, 9.98. $C_{20}H_{26}$. Calculated %: C 90.01; H 9.87.

Synthesis of 2,5,5-trimethyl-2-phenyl-4-hexanol (VI). $\beta$-Phenylisovaleric acid with m. p. 59° was obtained in 81% yield by passage of gaseous $CO_2$ through tert-butylbenzene $\beta$-(magnesium chloride). The literature [1] reports m. p. 58-59°. A solution of 150 g of the acid in 250 ml chloroform was added with vigorous stirring to 430 g $PCl_5$. Considerable heat was generated. After the acid had been added, the reaction mixture was stirred for another 12 hrs and with heating to 50° during the final 6 hrs. 160 g $\beta$-phenylisovaleryl chloride (XIV) was obtained.

Tert-butyl magnesium chloride prepared from 139 g tert-butyl chloride and 48 g Mg was added at 3° in the course of an hour to an ethereal solution of 142 g acid chloride (XIV). After the addition was completed, the mixture was stirred for another 2 hrs. The reaction gave 89 g of alcohol (VI). Found 0.975 OH group per molecule of alcohol.

## SUMMARY

1. The Grignard reagent from 1-chloro-2-methyl-2-phenylpropane — tert-butylbenzene $\beta$-(magnesium chloride) — reacts in the normal manner with aldehydes to form secondary alcohols in a yield of 53-73%.

2. The same Grignard reagent reacts with ketones to form tertiary alcohols in considerably lower yields (22-37%), since the ketones are partly reduced by it to secondary alcohols.

3. Reaction of tert-butylbenzene $\beta$-(magnesium chloride) with methyl formate goes mainly according to the normal mechanism with formation of secondary alcohol or its formic ester. With ethyl acetate the reaction only goes to the stage of formation of ketone which is then reduced to secondary alcohol and is esterified.

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# INVESTIGATIONS ON CONJUGATED SYSTEMS

## XCII. SEQUENCE OF ADDITION OF IODINE TO VINYLACETYLENIC HYDROCARBONS*

A. A. Petrov, Iu. I. Porfir'eva, T. V. Iakovleva, and K. S. Mingaleva

In preceding papers it was shown that the sequence of addition of bromine to vinylacetylenic hydrocarbons depends on their structure. Whereas unconjugated vinylacetylenes and vinylalkylacetylenes add on bromine at the double bond, unsubstituted vinylacetylene and alkenylacetylenes add bromine predominantly in the 1,4-position with formation of allenic halo derivatives. This behavior was attributed to changes in distribution of the electronic density in the conjugated system under the influence of radicals [1-5].

It was interesting to compare the sequence of addition of different halogens to vinylacetylenic hydrocarbons. We know that in the case, for example, of butadiene, iodine adds on only in the 1,4-position, whereas bromine, and more so chlorine, give considerable quantities of 1,2-products [6]. With this objective we also investigated the sequence of addition of iodine to vinyl-, vinylmethyl-, vinylethyl-, propenyl- and allylmethylacetylenes. The literature contains data only for the reaction of vinylacetylene with iodine, and the structure of the adduct was not elucidated [7].

All of the reactions of this class that we investigated were considerably speeded up by light, so that a radical mechanism is definitely involved. Iodine added very slowly in the dark.

The resulting diiodides were heavy oils which were colored by iodine. Their structure was determined through the infrared spectra.**

The spectrum of diiodovinylacetylene contains strong frequencies of a conjugated system of double bonds ($1616 \text{ cm}^{-1}$) and of the vinyl grouping (926, 966 and $6060 \text{ cm}^{-1}$). There was no trace of the frequencies of about 2100 and $3300 \text{ cm}^{-1}$ which characterize a terminal acetylenic grouping. Nor did the spectrum contain frequencies characteristic of the allenic system ($1960 \text{ cm}^{-1}$). The neighboring weak frequency of $1920 \text{ cm}^{-1}$ is observed in the spectra of many dienic compounds. Strong absorption at $760 \text{ cm}^{-1}$ bears witness to the cis-configuration of at least the greater part of the product.

It has thus been established that iodine adds onto vinylacetylene at the acetylenic bond.

The same conclusions are reached when we consider the spectra of the diiodo derivatives of vinylmethyl and vinylethylacetylenes. Here the conjugated system of double bonds is associated with the extremely intense $1603 \text{ cm}^{-1}$ frequency, and the vinyl group has strong frequencies at 917 and $965 \text{ cm}^{-1}$, as well as a characteristic overtone at $6060 \text{ cm}^{-1}$. Very weak absorption is observed in the normal region of absorption of disubstituted acetylenes, and this is probably an overtone. The $1960 \text{ cm}^{-1}$ frequency is absent from the spectrum. Consequently, the sequence of addition of iodine to vinylalkylacetylenes does not differ from that in the case of unsubstituted vinylacetylene.

Apart from the strong bands due to the $-CH=CH-$ grouping (947 and $1640 \text{ cm}^{-1}$), the spectrum of diiodopropenylacetylene also contains a weak band at $1971 \text{ cm}^{-1}$ which is suggestive of the presence of a very small

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* Enynic compounds. XXI.

** Investigations were carried out both on the distilled substances and on products obtained by removal of the solvent and starting hydrocarbon from the reaction mixture in vacuo at a temperature not exceeding 20°. The spectra of the latter contained many weak frequencies in the region above $2000 \text{ cm}^{-1}$. No differences in position and intensity of the principal frequencies were observed. Distillation is therefore not accompanied by isomerization.
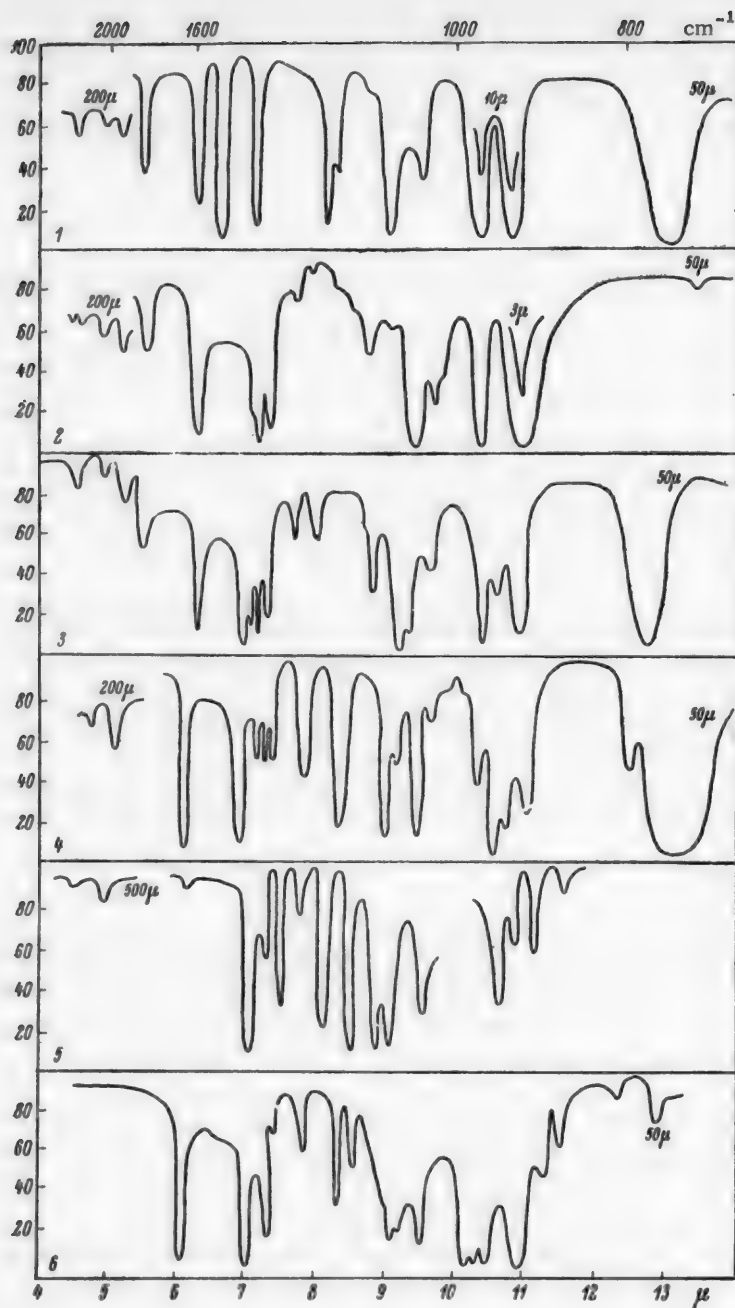
Infrared transmission spectra of diiodo compounds. 1) Vinylacetylene; 2) vinylmethyl-
acetylene; 3) vinylethylacetylene; 4) propenylacetylene (2nd fraction); 4) allyl-
methylacetylene (crystalline product with m. p. 65°); 6) allylmethylacetylene (liquid).

quantity of 1,4-adduct in the diiodo derivative. The 2102 $cm^{-1}$ frequency can be assigned to the valence vibra-
tion of the terminal acetylenic bond, but the usually very much more intense frequency of the valence vibrations
of the acetylenic hydrogen is entirely absent. The frequency at about 2100 $cm^{-1}$ is therefore an overtone.

It has thus been established that conjugated vinylacetylenes add on iodine at the acetylenic bond regardless of the structure.

Iodine adds on to allylmethylacetylene with great facility at both of the multiple bonds: the main product of the reaction when equimolar quantities of iodine and hydrocarbon are mixed is the tetraiodo compound. No tetraiodo compound was detected when conjugated vinylacetylenes were reacted, evidently due to steric hindrance. Two diiodo compounds were formed in addition to the tetraiodo compound: a liquid and a crystalline substance. The spectrum of the liquid contains a strong double-bond band (1640 cm$^{-1}$); in this region the spectrum of the solid substance exhibits only weak absorption.

The observed differences in the sequence of addition of bromine and iodine to vinylacetylenic hydrocarbons are evidently associated with differences in reaction mechanisms: bromine adds on by ionic or molecular mechanism and iodine by a well-marked radical mechanism.

Selective addition of atomic iodine at the acetylenic bond is determined in our opinion by the greater stability of the transition complex formed in this case. Interaction of a free electron of the iodine atom with the $\pi$-electrons of the triple bond can result in conjugation of this electron with the entire enynic system. Such a conjugation does not occur, however, when the site of addition is the double bond.

Hydrogenation of vinylacetylenic hydrocarbons is most probably also accompanied by radical addition of hydrogen atoms, and as in the case of iodine addition to the reaction takes place at the actylenic bond [8].

## EXPERIMENTAL

### Addition of Iodine to Vinylacetylenic Hydrocarbons

Vinylacetylene. A solution of 20 ml of vinylacetylene in 30 ml ethyl chloride and 50.8 g iodine were exposed for several hours in diffused light in a closed vessel which was shaken periodically. After decolorization had occurred, the ethyl chloride was evaporated off and the residue was distilled in vacuo. The following fractions were obtained: 1st, to 84°, 3.7 g; 2nd, 84-85°, 49 g; residue 3.0 g.

The following constants were found for 1,2-diiodo-1,3-butadiene*:

B. p. 84-84.5° (5 mm), $d_4^{20}$ 2.5652, $n^{20.1}\alpha$ 1.7082, $n^{21.7}$D 1.7165. $MR_\alpha$ 46.51; calc. 43.90. Found %: I 82.47, 82.55. $C_4H_4I_2$. Calculated %: I 82.98.

Infrared spectrum ** (cm$^{-1}$): 763 very strong, 926 very strong, 966 very strong, 1056 medium, 1103 very strong, 1173 very weak, 1202 medium, 1232 strong, 1404 very strong, 1524 very strong, 1616 strong, 1840 medium, 1920 weak, 2035 weak, 2204 very weak, 2849 weak, 2921 strong, 2967 very strong, 3001 medium, 3050 strong, 3082 very strong.

Vinylmethylacetylene. Under the same conditions, 25 g iodine and 8 g vinylmethylacetylene gave a product which on distillation in vacuo (5 mm) yielded the following fractions: 1st, to 94°, 2.5 g; 2nd, 94-95°, 24.5 g; residue 2.7 g.

The following constants were found for 2,3-diiodo-1,3-pentadiene:

B. p. 94-94.5° (5 mm), $d_4^{20}$ 2.3781, $n^{20}\alpha$ 1.6886, $MR_\alpha$ 51.34; calc. 48.50. Found %: I 79.44. $C_5H_6I_2$. Calculated %: I 79.34.

Infrared spectrum (cm$^{-1}$): 760 very weak, 917 very strong, 965 very strong, 1030 strong, 1064 very strong, 1102 very weak, 1144 medium, 1270 weak, 1298 weak, 1373 very strong, 1401 very strong, 1603 very strong, 1830 medium, 1920 weak, 2027 weak, 2092 very weak, 2162 very weak, 2239 weak, 2713 medium, 2790 medium, 2824 strong, 2908 very strong, 2954 strong, 2977 strong, 3003 strong, 3105 very strong.

The reaction went to the extent of 10% when a chloroform solution of the hydrocarbon and iodine with a concentration of 0.1 mole/liter stood in the dark for 3 days. In diffused light the reaction was completed in 3 hrs.

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* Diiodovinylacetylene is reported [7] to have b. p. 91.5-92° (3 mm).
** The infrared transmission spectra were plotted with the IKS-12 spectrograph with an LiF prism in the region up to 5.5 $\mu$, and subsequently with a NaCl prism.

<u>Vinylethylacetylene.</u>  The product obtained from 50.8 g iodine and 17 g hydrocarbon in 30 ml ethyl chloride gave the following fractions on distillation in vacuo (5 mm): 1st, to 101°, 5.0 g; 2nd, 101-103°, 37.7 g; residue 5.2 g.

The following constants were found for 2,3-diiodo-1,3-hexadiene:

B. p. 101-103° (5 mm), $d_4^{20}$ 2.2175, $n^{20.1}\alpha$ 1.6639, $MR_\alpha$ 55.85;  calc. 53.09. Found %: I 75.88, 76.66. $C_6H_8I_2$. Calculated %: I 76.01.

Infrared spectrum (cm$^{-1}$):  787 very strong, 916 very strong, 947 weak, 964 very strong, 1035 weak, 1072 very strong, 1088 very strong, 1146 strong, 1255 medium, 1308 medium, 1378 strong, 1402 very strong, 1421 strong, 1453 very strong, 1606 very strong, 1830 medium, 1920 weak, 2045 very weak, 2220 weak, 2814 weak, 2848 medium, 2865 very strong, 2925 very strong, 2954 very strong, 3000 medium, 3095 strong.

<u>Propenylacetylene.</u>  12.7 g iodine and 3.8 g hydrocarbon gave 15 g of a substance which was resolved into the following fractions on distillation: 1st, to 93°, 1.0 g; 2nd, 93.5-94.5°, 3.5 g; 3rd, 95-97°,4.5 g; 4th, 97-102°, 3.1 g; residue 1.2 g.

The following constants were found for the 2nd fraction:

$d_4^{20}$ 2.3410, $n^{20.1}\alpha$ 1.6827, $n^{20}D$ 1.6860, $MR_\alpha$ 51.81;  calc. 48.50. Found %: I 78.46, 78.62. $C_5H_6I_2$. Calculated %: I 79.34.

Infrared spectrum (cm$^{-1}$):  720 very strong, 801 weak, 910 strong, 931 strong, 947 very strong, 970 strong, 1035 weak, 1060 very strong, 1090 medium, 1110 very strong, 1205 very strong, 1280 strong, 1360 medium, 1377 medium, 1402 medium, 1453 very strong, 1640 very strong, 1971 medium, 2102 weak, 2841 strong, 2860 medium, 2901 very strong, 2930 very strong, 2964 strong, 3012 strong, 3060 very strong, 3080 very strong.

The compound did not lose iodine when stood with 5% alcoholic KOH for 2 hrs.

Found for the 3rd fraction:

$d_4^{20}$ 2.3427, $n^{20}\alpha$ 1.6836, $MR_\alpha$ 51.73;  calc. 48.50.

Found for the 4th fraction:  $d_4^{20}$ 2.3470.

Found %: I 79.66. $C_5H_6I_2$. Calculated %: I 79.34.

The compound loses about 25% iodine when stood with 5% KOH solution.

The intensity and position of the frequencies associated with the multiple bonds do not differ from those given for the 2nd fraction.

<u>Allylmethylacetylene.</u>  Fairly rapid decolorization occurred when a solution of 8 g hydrocarbon in 30 ml ethyl chloride was shaken with 25 g iodine, and a crystalline precipitate was formed (16 g, 55% of the total reaction products).  The latter was separated and recrystallized from carbon tetrachloride. M. p. 103-105°. Sparingly soluble in the usual organic solvents.

Found %: I 87.25, 85.76. $C_6H_8I_4$. Calculated %: I 86.37.

5 g of a crystalline substance came down from the liquid after evaporation.

M. p. 65° (from CCl$_4$).  Very much more soluble than the tetraiodo compound.

Found %: I 78.07, 78.10. $C_6H_8I_2$. Calculated %: I 76.01.

Infrared spectrum (cm$^{-1}$) in CCl$_4$:  886 weak, 902 strong, 925 medium, 943 strong, 1054 strong, 1107 very strong, 1135 very strong, 1184 very strong, 1230 very strong, 1290 medium, 1355 strong, 1382 medium, 1427 very strong, 1644 very weak (?), 2052 very weak, 2240 weak, 2734 medium, 2815 medium, 2854 strong, 2888 strong, 2917 very strong, 2964 strong, 3028 medium, 3092 weak.

The oil left after the crystals had been separated was distilled in vacuo (4 mm) to give the following fractions: 1st, to 97°, 2 g; 2nd, 97-98°, 6.1 g; residue, 3.5 g. All of these fractions partly crystallized on standing. The crystals deposited from the 2nd fraction were collected (1.3 g, m. p. 65°), and the liquid was examined. The following data were obtained:

$d_4^{20}$ 2.1810, $n_{\alpha}^{20.2}$ 1.6395, $MR_{\alpha}$ 55.13; calc. 53.09. Found %: I 75.25, 75.15. $C_6H_8I_2$. Calculated %: I 76.01.

Infrared spectrum $(cm^{-1})$: 778 weak, 811 weak, 871 weak, 888 medium, 920 very strong, 964 very strong, 976 very strong, 988 very strong, 1055 strong, 1103 strong, 1120 very weak, 1180 medium, 1202 strong, 1284 medium, 1292 weak, 1350 very weak, 1375 strong, 1427 very strong 1640 very strong.

The crystalline diiodo compound constituted 28% and the liquid 17% of the total product.

## SUMMARY

1. The sequence of addition of iodine to five vinylacetylenic hydrocarbons was investigated: vinyl-, vinylmethyl-, vinylethyl-, propenyl- and allylmethylacetylenes.

2. It was shown that, except with the last compound, iodine adds on at the acetylenic bond. It adds on to allylmethylacetylene at both of the multiple bonds with considerable formation of the tetraiodo compound.

3. The reaction is accelerated by light, and therefore a chain radical mechanism is involved.

4. It is suggested that the difference in the sequence of addition of iodine and bromine to vinylacetylenic hydrocarbons is associated with different mechanisms of addition (an ionic mechanism was previously proposed for addition of bromine).

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* Original Russian pagination. See C. B. translation.

# INVESTIGATIONS ON CONJUGATED SYSTEMS

## XCIII. THE SEQUENCE OF ADDITION OF ALKYL HYPOBROMITES TO VINYLALKYLACETYLENES*

### A. A. Petrov, Iu. I. Porfir'eva, and G. I. Semenov

In preceding communications we showed that vinylalkylacetylenes add on hydrogen [1] and iodine [2] at the triple bond, bromine [3] and alkyl hypobromites [4] at the double bond, and hydrogen halides [5] predominantly in the 1,4-position. These differences in the sequence of addition of bromine and iodine were thought to be due to differences in reaction mechanism (ionic in one case and radical in the other). Concerning the differences in order of addition of bromine and hydrogen bromide, these were correlated with the inability of the triple bond to give a transition $\pi$-complex with bromine, whereas hydrogen halides form such complexes with facility.

The structure of the products of addition of all of these substances to vinylacetylenes was determined by chemical methods and with the help of their infrared spectra (except in the case of products of addition of alkyl hypobromites, for which the second technique was not used). Since infrared spectra are the most sensitive and reliable means of determination of the structure of isomeric products of addition of various substances to vinyl-acetylenic hydrocarbons [6], we repeated the experiments on addition of alkyl hypobromites to vinylalkyl-acetylenes and investigated the spectra of the resulting bromoethers and the products of their dehydrobromination.
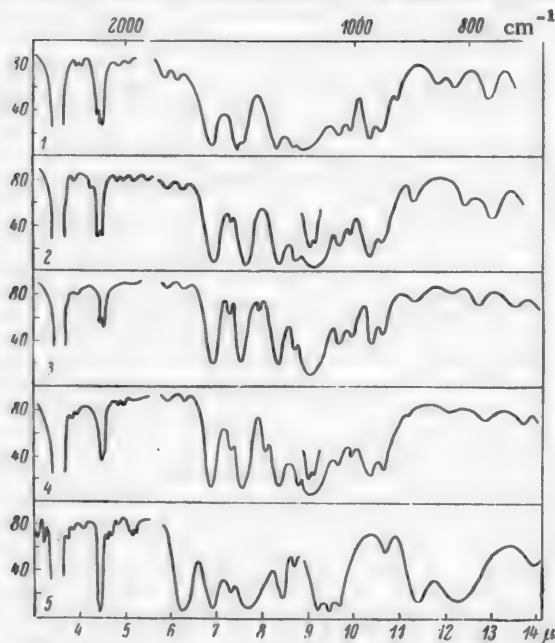


Infrared transmission spectra. 1) Bromoether from vinyl-methylacetylene, 2) bromoether from vinylethylacetyl-ene (obtained by the action of bromine on an alcoholic solution of hydrocarbon), 3) bromoether from vinylpro-pylacetylene, 4) bromoether from vinylbutylacetylene, 5) enol ether obtained from vinylmethylacetylene.

The infrared spectra of all of the bromoethers (see diagram) contained a strong triple bond band, usually consisting of several frequencies in close proximity with a maximum at 2247 or 2257 cm$^{-1}$. Frequencies charac-teristic of dienic (1625 cm$^{-1}$) and allenic (1965 cm$^{-1}$) groupings were very weakly represented in the spectra. Slight absorption in the 1700 cm$^{-1}$ region is very fre-quently observed in the spectra of acetylenic compounds [7]. The ether grouping evidently corresponds to the 1100-1114 cm$^{-1}$ doublet. In the 900-1000 cm$^{-1}$ region all the spectra contain two intense bands at ~ 950 and 970 cm$^{-1}$ and a weak band forming an overtone on a preced-ing band at ~ 917 cm$^{-1}$. The 917 and 970 cm$^{-1}$ frequencies might be associated with the presence of a vinyl group in the bromoethers, although in the 1600-1640 cm$^{-1}$ region and at 6100 cm$^{-1}$ (overtone) the bromoethers do not exhibit the strong absorption characteristic of this group. The frequencies are most probably associated mainly with vibrations in saturated radicals.

Consequently, the infrared spectra confirm the earlier conclusions to the effect that alkyl hypobromites add on almost exclusively at the olefinic bond. At the

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same time they indicate that acetylenic bromoethers are not the sole products of the reaction: very small quantities of 1,3-dienic and allenic bromoethers are also formed.

Formation of a small quantity of allenic bromoethers was confirmed by the infrared spectra of the enolic ethers — products of dehydrobromination of the original bromoethers. These spectra contain a weak frequency at about 3300 cm$^{-1}$ which is characteristic of the hydrogen of a terminal acetylenic grouping. Formation of an ether from such a grouping is only possible from an allenic bromoether according to the equation R—COR=C=CH— —CH$_2$Br $\rightarrow$ R—COR=C=C=CH$_2$ $\rightarrow$ R—COR=CH—C≡CH.

The intensity of the 3300 cm$^{-1}$ frequency falls off sharply on passage from vinylmethylacetylene to vinylethylacetylene, and is hardly perceptible in the higher homologs. Proof that the 3300 cm$^{-1}$ frequency is associated with the stretching frequency of the acetylenic hydrogen is afforded by its disappearance after treatment of the enolic ethers with ammoniacal silver oxide. The enolic ethers are then recovered to the extent of over 90%. Consequently, the content of impurities must be much below 10%. A precipitate of silver derivative only comes down in the case of the enolic ether prepared from vinylmethylacetylene. Very slight turbidity is observed in other cases.

We effected addition of alkyl hypobromites to vinylalkylacetylenes by two methods: a) by the action of benzenedibromosulfonamide on alcoholic solutions of the hydrocarbons; b) by the action of a solution of bromine in methanol on a solution of the hydrocarbon in the same alcohol. The infrared spectra failed to reveal any significant differences in the structures of the resulting bromoethers. The second method gave compounds with excess of bromine due to the presence of a small quantity of dibromides.

## EXPERIMENTAL

Methods of preparation of the hydrocarbons, their constants and the method of preparation of the bromoethers with the help of benzenedibromosulfonamide were described in previous communications [3, 4]. In this paper (see Table 1) we again present the constants of some of the bromoethers (since they were obtained in large quantities and the boiling point previously found for the bromoether from vinylpropylacetylene was erroneous [4]).

TABLE 1

| Substance | Boiling point (10 mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | |
|---|---|---|---|---|---|
| | | | | found | calc. |
| CH$_2$Br—CH(OCH$_3$)—C≡C—CH$_3$ | 65—66° | 1.3647 | 1.4880 | 37.38 | 37.31 |
| CH$_2$Br—CH(OCH$_3$)—C≡C—C$_2$H$_5$ | 77—78 | 1.2900 | 1.4804 | 42.11 | 41.93 |
| CH$_2$Br—CH(OCH$_3$)—C≡C—C$_3$H$_7$ | 88—89 | 1.2415 | 1.4782 | 46.78 | 46.55 |
| CH$_2$Br—CH(OCH$_3$)—C≡C—C$_4$H$_9$ | 105—106 | 1.2016 | 1.4758 | 51.42 | 51.17 |

The hydrocarbons were treated with an alcoholic solution of bromine under the following conditions.

A methanol solution of 0.2 mole bromine (cooled to −5 to −10°) was added dropwise with intensive stirring to a solution of 0.25 mole vinylethylacetylene in 100 ml alcohol (cooled to the same temperature). When the reaction was completed, the mixture was diluted with water, and the layer of bromoether was collected, washed with saturated CaCl$_2$ solution and distilled. There was obtained 25 g product which yielded the following fractions on distillation in vacuo (10 mm): 1st, to 76°, 1.5 g; 2nd, 76-78°, 16.8 g; 3rd, 78-80°, 5 g; 4th, 80-82°, 3 g; residue, 7 g. Yield of bromoether (fractions 2 and 3) 57%.

The main fraction had: d$_4^{20}$ 1.3164, n$^{20}$D 1.4848.

Found %: Br 44.33, 44.27. C$_7$H$_{11}$OBr. Calculated %: Br 41.92.

The analytical data indicate that the product is contaminated with about 10% of dibromide.

Treatment of the bromoether with alcoholic alkali gave the enol ether with the following constants: b. p. 53-54° (20 mm), d$_4^{20}$ 0.8894, n$^{20}$D 1.4685.

## TABLE 2

Infrared Transmission Spectra of Bromoethers $CH_2Br-CH(OCH_3)-C\equiv C-R$ with the Following Values of R

| $CH_3$ | $C_2H_5$ | $C_3H_7$ | $C_4H_9$ |
|---|---|---|---|
| 2294 strong | 2288 * strong | 2278 strong | 2278 * strong |
| 2268 strong | 2269 strong | 2257 strong | 2257 strong |
| 2247 strong | 2247 strong | 2237 * strong | 2237 * strong |
| 1965 v. weak | 1965 v. weak | 1965 v.weak | 1965 v. weak |
| 1709 weak | 1715 weak | 1710 weak | 1695 weak |
| 1626 weak | 1609 weak | 1608 weak | 1605 weak |
| 1456 strong | 1456 strong | 1460 strong | 1466 strong |
| — | 1377 strong | 1381 strong | 1377 *strong |
| 1346 strong | 1330 strong | 1335 strong | 1333 strong |
| 1321 strong | 1318 strong | | — |
| 1270 * med. | 1270 * med. | 1276 med. | 1248 * med. |
| 1209 strong | 1206 strong | 1206 strong | 1206 strong |
| 1163 strong | 1156 *strong | 1156 * strong | 1156 *strong |
| 1114 v. strong | 1114 v. strong | 1114 v. strong | 1114 v. strong |
| 1100 v. strong | 1100 *v.strong | 1100 * v.strong | 1100 * v. strong |
| 1038 strong | 1039 strong | 1039 strong | 1040 strong |
| 1012 strong | 1006 strong | 1006 strong | 1006 strong |
| 971 strong | 974 strong | 968 strong | 971 strong |
| 950 strong | 950 strong | 947 strong | 947 strong |
| 917 med. | — | 917 weak | — |
| 850 med. | 888 med. | 888 weak | — |
| 821 med. | 808 weak | 826 weak | — |
| 781 med. | 777 med. | 793 med. | 781 med. |
| — | — | 741 med. | 734 med. |

Note. Starred frequencies are overtones on other (stronger) frequencies.

Its specific gravity and refractive index are slightly higher than for the pure substance due to the pressure of bromide formed by dehydrobromination of dibromide which was contained in the original bromoether.

The infrared spectra were obtained with the IKS-2 spectrograph, using a lithium fluoride prism down to 5.5 $\mu$ and subsequently a sodium chloride prism. The thickness of the layer was 0.1 mm and less.

The spectra of the purified enolic ethers were closely studied in one of the preceding communications [8]. Data for the spectra of the bromoethers are presented in Table 2 and plotted in the diagram.

## SUMMARY

1. A study of the infrared spectra confirmed the previous conclusion as to the preferential addition of alkyl hypobromites to vinylalkylacetylenes (by the action of benzenedibromosulfonamide on alcoholic solutions of the hydrocarbons) at the double bond.

2. It was shown that along with this main direction of the reaction, there is partial addition of alkyl hypobromites at the acetylenic bond and in the 1,4-position. With increasing size of the alkyl radical of the hydrocarbon, the last direction of the reaction becomes less pronounced.

3. It was established that the addition reaction goes in the same direction when bromine acts on alcoholic solutions of vinylalkylacetylenes.

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# THE VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE
## AND ITS HOMOLOGS

### III. STUDY OF THE PROCESS OF CATALYTIC HYDRATION OF ACETYLENE
### OVER SOME SOLID CATALYSTS

Iu. A. Gorin and I. K. Gorn

Information on the hydration of acetylene to acetaldehyde in the gas phase over solid catalysts has been supplied mainly by the patent literature without any discussion of theoretical considerations that might enable correlation of the activity of the catalysts with their nature and properties. The lack of such data must be attributed to the empirical basis of selection of the majority of the catalysts put forward in patents. There has been an entire lack of systematic work. Of the large number of substances proposed, we can only mention some of the more common ones: phosphoric acid and various phosphates (in particular copper phosphate , zinc phosphate and cadmium phosphate), sometimes other salts of the same metals, and compounds of tungsten, molybdenum and vanadium [1-3]. The mechanism of the hydration of acetylene over solid catalysts has been very inadequately investigated, although an insight into this mechanism might be expected to facilitate the correct choice of catalyst. There are only a few publications dealing with the fundamentals of this reaction, and they do not contain any detailed considerations.

Boswell and Dilworth [4] studied the catalytic action of alumina in a number of hydration and dehydration reactions (including the hydration of acetylene) and attribute the effect to surface films of ions of dissociated water which cover the catalyst particles. Iakubovich and others [5] studied the activating effect of phosphates of zinc and copper on phosphoric acid supported on active carbon. They apparently suggested that the copper salt activates the process when it is in a state of higher valence since they consider the reduction to the lower valence stage to be one of the possible causes of deactivation of the catalysts during the reaction. They found the lower oxide in the spent catalyst.

An insight into the mechanism of the reaction at solid catalysts can be obtained from the ideas propounded by some investigators on the liquid-phase process. A. L. Klebanskii and V. D. Titov [6] investigated the hydration of acetylene in phosphoric acid solution in presence of salts of zinc, silver and mercury; they attribute the activating action of these salts to their ability to form complexes with acetylene, the molecule of the latter becoming activated on ionization of the complex. The authors emphasize that the activating action of such salts is especially conspicuous when the reaction is conducted in the vapor phase on solid supports. The theory of Klebanskii and Titov is an interesting one since the nature of the activation of acetylene may be the same in the conditions of liquid-phase and gas-phase hydration. The actual occurrence of ionization of acetylene in solutions under the action of lower copper salts was subsequently confirmed by the work of A. L. Klebanskii, I. M. Dolgoplosk, and Z. F. Dobler [7, 8]. The authors associate the ready susceptibility of acetylene to ionization with the mobility of the π-electrons of the triple bond.

In the present work we studied the hydration of acetylene over solid catalysts containing various cations, since the development of cations capable of  activating the reaction can serve as a first step toward  the understanding of the mechanism of action of a catalyst. In order to exclude the influence of anions, we used only phosphates as catalyst. Along with this we investigated the catalytic action of some of those metals whose phosphates were found to be active catalysts.

## Special Features of the Electronic Structure of Phosphates Capable of Catalyzing the Hydration of Acetylene

Of the very large number of phosphates (neutral orthophosphates) only a few are capable of catalyzing the hydration of acetylene, namely the phosphates of copper, cadmium and zinc. A number of other phosphates are characterized by extremely low activity or by substantial absence of activity. Our experimental results are presented in the table (Nos. 1-10).

Activity of Some Phosphates as Catalysts of the Hydration of Acetylene to Acetaldehyde

| No. | Phosphate cation | Tempera- ture | Degree of conversion of acetylene (in %) | Yield of acetaldehyde (mole%) | |
|---|---|---|---|---|---|
| | | | | on acetyl- ene passed through | on acetylene converted |
| 1 | Copper (ic) | 250—300° | 88.0 | 55.7 | 63.2 |
| 2 | Cadmium | 390—400 | 73.8 | 62.0 | 83.8 |
| 3 | Zinc* | 390—400 | 52.2 | 48.3 | 92.7 |
| 4 | Calcium | 390—400 | 3.3 | 1.2 | — |
| 5 | Strontium | 390—400 | 0.0 | 0.0 | — |
| 6 | Barium | 390—400 | 1.6 | 0.0 | — |
| 7 | Aluminum | 390—400 | 0.0 | 0.0 | — |
| 8 | Iron (ic) | 390—400 | 6.1 | 1.3 | — |
| 9 | Nickel | 390—400 | 6.0 | 4.2 | — |
| 10 | Tin | 390—400 | 0.0 | 0.0 | — |
| 11 | Mercury (20 wt.% of mer- curic phosphate on cal- cium phosphate) | 320—330 | 4.8 | 2.4 | — |
| 12 | Silver (20 wt.% of silver phosphate on calcium phosphate) | 200—300 | 6.7 | 2.6 | — |
| 13 | Silver (phosphate) | 200—300 | 44.6 | 35.2 | 78.8 |

* The catalytic properties of zinc phosphate were previously studied by Iu. A. Gorin, A. N. Makashina and others [9].

Phosphates of copper, cadmium and zinc differ in respect to the nature of their catalytic action. The overall catalytic activity of copper phosphate, determined from the degree of conversion of acetylene, is so high that hydration of acetylene proceeds in its presence at a relatively low temperature. At the same time the catalyst has poor selectivity, the yield of acetaldehyde (reckoned on reacted acetylene) being low, since secondary reactions play an important part (condensation of acetaldehyde to crotonaldehyde and oily products, and polymerization of acetylene to cuprene). The polymers are the cause of the rapid choking of the reaction tube.

Cadmium phosphate is less active than copper phosphate, the hydration of acetylene over $Cd_3(PO_4)_2$ requiring a higher temperature (reaction starts at 330-350°), although this catalyst is very much more selective and is more stable.

The least active of the three catalysts is zinc phosphate. It is evident that the difference in behavior of the phosphates during hydration of acetylene must be governed by the character of their cations. From this standpoint the cations of the phosphate which are active catalysts must possess some property in common. We established such a general property in the structure of the electron shells of the elements Cu, Zn and Cd [10]. In each of these elements one or two of the electrons of the s subgroup are in the outer shell. The d subgroup of the preceding (penultimate) orbital is then completely filled by ten electrons (Cu — $3d^{10}4s$, Zn — $3d^{10}4s^2$, Cd — $4d^{10}5s^2$). To the same elements whose d subgroup is not completely filled, even when the outer shell contains s-electrons, correspond phosphates which are characterized by low activity in the hydration of acetylene, as can be seen with reference to the phosphates of iron and nickel (Fe — $3d^6 4s^2$, Ni — $3d^8 4s^2$). d-Electrons are also absent from the vicinity of the outer s-electrons in the elements Al, Ca, Sr, Ba (Al — $3s^2 3p$, Ca — $3p^6 4s^2$, Sr — $4p^6 5s^2$, Ba — $5p^6 6s^2$), and this structure likewise coincides well with the absence of catalytic activity from their phosphates. It is true that in the salts we are not dealing with atoms of Cu, Cd or Zn, but with ions; nevertheless the completion of the number of electrons of the d subgroup is evidently the decisive factor.

On the other hand, subsequent filling of the outer orbital with electrons (appearance of p-electrons) also leads to loss of activity, as is observed in the case of tin phosphate ($Sn - 4d^{10} 5s^2 5p^2$).

The above-noted feature of the structure of the outer orbitals of the electron shell characteristic not only of Cu, Cd and Zn, but also of Ag, Au and Hg ($Ag - 4d^{10} 5s$, $Au - 5d^{10} 6s$, $Hg - 5d^{10} 6s^2$). There are no other elements of similar structure in the periodic system. It was therefore of interest to compare the catalytic action in acetylene hydration of phosphates of these elements with the action of phosphates of copper, cadmium and zinc. Since the literature contains no information about the possibility of preparation of gold phosphates, we studied the catalytic properties of only mercury and silver phosphates (table, Nos. 11-13).

For convenience in testing, we used mercuric phosphate in admixture with calcium phosphate which served as a carrier.* During the reaction it was completely reduced to metallic mercury which condensed in the cold part of the reaction tube.

Silver phosphate was tested both in admixture with a carrier (calcium phosphate) and in its absence. It, too, suffered decomposition, as was especially conspicuous in experiments in which silver phosphate was used alone (the spent catalyst consisted of free phosphoric acid and metallic silver). It should be pointed out that decomposition of silver phosphate was avoided by starting the test in both cases at low temperature (200°), and only in the event of complete inertness of the catalysts was the temperature gradually raised to 300°. The reaction only commenced at 285° when silver phosphate was used without a carrier ; substantially no conversion of acetylene was observed when silver phosphate was mixed with calcium phosphate.

The lack of activity of mercuric phosphate can be easily explained by the reduction to mercury which, as we know from the liquid-phase process, does not catalyze the hydration of acetylene. From this standpoint the catalytic effect of silver phosphate alone (which is likewise reduced to metal) is anomalous. This anomaly, however, is only an apparent one, for the catalytic effect must here be attributed to the phosphoric acid which is liberated on breakdown of the phosphate. Catalysts were found to be inert when the conditions were such that free phosphoric acid could not be present. This would apply in presence of a carrier (calcium phosphate, with which phosphoric acid reacts to form the catalytically inert pyrophosphate). Decomposition of the phosphate evidently only occurs at about 285°, for otherwise the commencement of reaction would have been observed at a lower temperature since phosphoric acid catalyzes the hydration of acetylene even at 130° [6]. Silver phosphate itself is evidently inactive at temperatures below 285°. These observations show that silver phosphate is scarcely suitable as a solid catalyst for the hydration of acetylene.

We checked the lack of catalytic activity of free metals in acetylene hydration in the case of zinc and cadmium. Zinc was tested at 390-400° in the form of dust pelleted with pulverized pumice. Whereas zinc phosphate is an active catalyst, the degree of conversion of acetylene in presence of zinc under the same conditions was only 6.9%. ** Metallic cadmium was tested in the form of dust at a lower temperature than was employed with zinc (the melting point of cadmium is 320.9°) and was likewise inactive. The inability of the free metals to catalyze the hydration of acetylene indicates that the reaction of the solid catalyst with acetylene has an ionic character. In view of the suggested possibility of formation of complexes of acetylene with copper salts in solutions [7], we suggest that ions of copper, cadmium and zinc in the solid catalyst lattice form complexes with acetylene at the catalyst surface at the expense of the $\pi$-electrons of the triple bond.

In an earlier communication [12] we proposed the mechanism of hydration of acetylene and some of its mono- and disubstituted derivatives which is based on the results and concepts obtained and developed in the present work. Formation of complexes necessary for activation of acetylene hydration evidently proceeds only when the electron cloud of the cations of the catalyst has a specific structure, and this structure also characterizes the three cations in question. This is equally true of the mercury cation. It is true that mercuric phosphate cannot be used as a gas-phase catalyst due to its great susceptibility to reduction to metal under the reaction conditions, but mercury salts are generally known to be active in the liquid-phase process.

In this connection it is highly probable that only bivalent cations can activate the hydration of acetylene. This is not so, for example, in the case of its polymerization. This view is supported by the well-known fact that

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* Calcium phosphate has been employed as a good carrier for various acetylene hydration catalysts [11].
** The slight activity of zinc was probably due to formation of some zinc oxide which is known to catalyze the hydration of acetylene.

mercurous salts do not catalyze this reaction in the liquid phase. One of us [13] has drawn attention to the poor activity of solid catalysts containing cuprous salts. It may be thought that a condition for formation of complexes capable of activating the hydration of acetylene both in solutions and on solid catalysts is the presence of a charge of specific magnitude on the cations along with the above-mentioned structure of the electron cloud. When the charges are lower, i. e., in the case of univalent cations, the required degree of polarization or ionization of acetylene is not attained. On this basis the silver cation cannot activate the hydration of acetylene even if we ignore the facility of breakdown of silver phosphate.

If the ideas that we have put forward about the relation between a specific structure of the electron cloud of cations and the ability of the salts of these cations to activate the hydration of acetylene are correct, then it follows that the number of suitable catalysts (salts) is indeed very small. Grave doubt must therefore be cast upon the claims in patent literature for the suitability as catalysts of numerous salts with other cations.

## EXPERIMENTAL

Phosphate catalysts were prepared by precipitation from solutions of the corresponding sulfates or nitrates by the action of solutions of di- or trisubstituted ammonium orthophosphate. The precipitates were filtered, washed free of soluble salts, dried at 100-110° and compressed to tablets in a laboratory hydraulic press. The tablets were then broken into 2-3 mm pieces. Mixed catalysts (silver phosphate or mercuric phosphate mixed with calcium phosphate) were prepared by mechanical mixing of the separately precipitated phosphates which had been pulverized and sieved through a 0.15 mm-mesh screen. Mixing was effected in suspension in water. The mixture was then filtered, dried and tableted. The catalyst consisting of zinc dust and pumice was prepared by mixing the powders in the dry state and then tableting. The cylinder acetylene employed in the tests was purified by washing with sodium hypochlorite solution. After purification, the gas contained 98% acetylene (determination by absorption in oleum).

Acetylene was hydrated in a quartz tube, diameter 25 mm and length 1 m, heated in an electric furnace. The amount of catalyst was 50 ml; the remaining space in the reaction tube was filled with pieces of quartz. Acetylene was admitted into the furnace from a gas-holder via a flowmeter, and water from a small buret. Reaction temperatures were measured with a thermocouple whose junction was in the center of the catalyst bed. The reaction products passed through a water condenser and were collected in a receiver cooled with ice. The gas, consisting mainly of unreacted acetylene, was washed free of aldehyde vapor in absorption bulbs containing hydroxylamine and collected in a gas-holder. The temperature of the experiments was usually 390-400°, the space velocity 150 liters/liter cat./hr, the dilution (by volume) of the acetylene with water vapor 1:10. Duration of the experiments 3-5 hrs. Aldehyde and aqueous-acetylenic condensate were determined with hydroxylamine hydrochloride. Unreacted acetylene in the gaseous reaction products was determined by absorption in oleum.

## SUMMARY

1. Several salts of phosphoric acid with various cations, as well as metallic zinc and cadmium, were examined as catalysts for the gas-phase hydration of acetylene to acetaldehyde.

2. It was shown that the action of solid catalysts of acetylene hydration bears an ionic character.

3. It was shown that the phosphate cations (Cu, Cd, Zn, Hg) which catalyze the hydration of acetylene are characterized by a specific structure of the electron cloud. Deviation from this structure involves loss of catalytic activity in this reaction.

4. The theory is advanced that activation of the hydration of acetylene is achieved only by bivalent cations.

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** See C. B. translation.

# INVESTIGATIONS ON POLYMETHYLENE RINGS

## XXXII. TRANSFORMATIONS OF CYCLOHEXENE IN CONJUGATED HALOGENATIONS AND DEHALOGENATIONS

### N. A. Domnin and V. A. Cherkasova

We have shown in a series of investigations that 1,3-cyclohexadienes and their substituted derivatives, likewise polyhalo derivatives of cyclohexane, are converted to the corresponding aromatic compounds under conditions of conjugated halogenation and dehalogenation [1]. Characteristic of these conversions is their irreversibility with formation of stable aromatic end products. These transformations are therefore analogous with Zelinskii's "irreversible catalysis."

Another characteristic feature of these transformations is the necessary presence of a source of bromine, which can be molecular bromine itself or a quoline polybromide, tetrabromo- and hexabromoethanes and other compounds rich in bromine and releasing it with facility.

We advanced a mechanism of conjugated halogenation and dehalogenation based on investigation of these reactions. Two variants were suggested: transformations with a relatively simple mechanism involving addition and scission of halogens or hydrogen halides, and transformations accompanied by intramolecular isomerizations. The first variant may be represented by the simplest conversion of 1,3-cyclohexadiene into benzene and bromobenzene in presence of polybromides of quinoline or of hexabromomethane and quinoline.
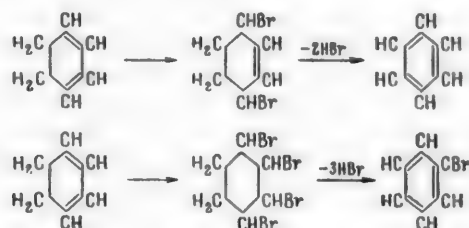


Another example is the conversion of 1,2-dibromo-1-cyclohexene into o-bromobenzene under the action of molecular bromine.
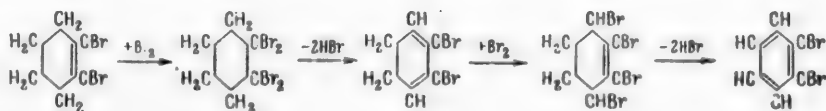


The second variant can be illustrated by the transformation of 1,2-dibromo-1-cyclohexene into bromobenzene under the action of bromine.
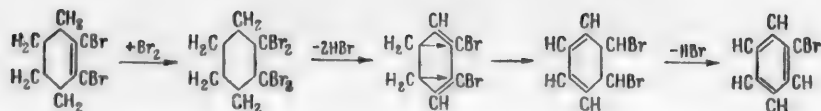
Another example is the transformation of 1-chloro-1,2-dibromocyclohexane into benzene under the action of quinoline.
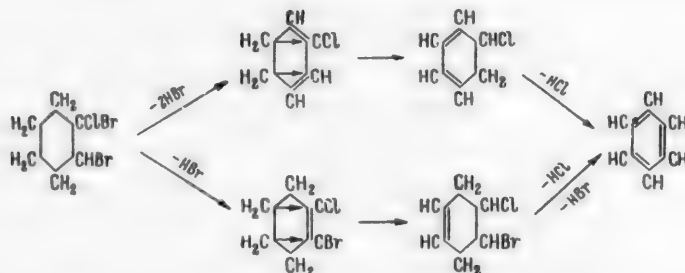
The mechanism of the first type of conversion can be considered proven, but that of the second type has remained unproven, since the migration of hydrogen atoms to the β-position has hitherto not been demonstrated. We can therefore advance another mechanism for the second type of conversion which involves cleavage and subsequent addition of hydrogen halide according to the scheme:
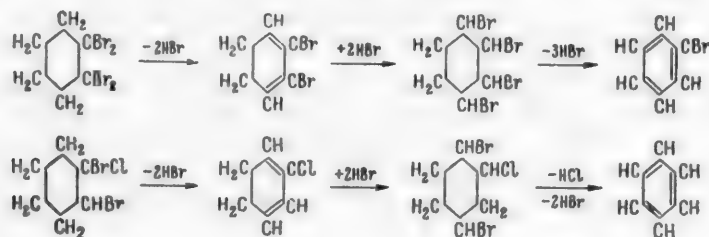
or a subsequent allylic rearrangement:
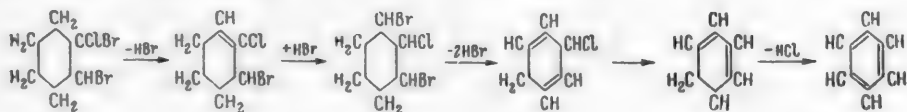
The above mechanisms of conjugated halogenation and dehalogenation take account of all of the known facts in this field. It must be remembered that there is a possibility of these reactions proceeding simultaneously in accordance with all of the suggested schemes. In connection with the further study of the mechanism of these reactions, it was of interest to investigate the transformations of cyclohexene under the conditions of conjugated halogenation and dehalogenation.

In the light of the foregoing considerations the reaction of cyclohexene with quinoline polybromides or of hexabromoethane and quinoline should proceed according to the scheme set forth below. Of all of the possible main products of these reactions, the only ones that are stable and permanent are benzene or its halogenated derivatives. All of the remainder — 1-bromo-1-cyclohexene, 1,2,2-tribromocyclohexene, 1,2-dibromo-1-cyclohexene, and 2-bromo-1,3-cyclohexadiene — will be intermediates and are most probably converted into bromobenzene and o-dibromobenzene or into benzene. Experiment confirmed this supposition. Benzene is formed when cyclohexene reacts with quinoline tetrabromide or with hexabromoethane in presence of quinoline.
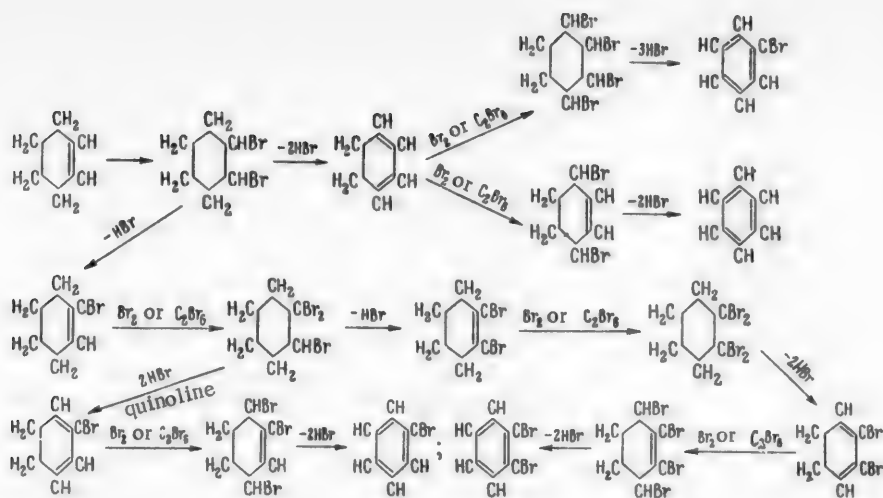
## EXPERIMENTAL

Reaction of cyclohexene with quinoline dibromide. Cyclohexene was prepared [2] by the action of sulfuric acid on cyclohexane. After careful fractionation, a fraction with b. p. 83-83.5° was selected. Quinoline dibromide was prepared from quinoline supplied by the Kharkov Chemical Reagent Works, serial number 50/28.

40 g quinoline dibromide was added through a reflux condenser to 8 g cyclohexene in a round-bottomed flask. The contents of the flask formed layers. The top layer was collected (20 g). It was the hydrate water of quinoline dibromide remaining after reaction of the dibromide with cyclohexene. A further small quantity of oil came down when water was added to the top layer. The oil was added to the main product (the lower layer). The latter was a brown, heavy oil (28 g), consisting of 1,2-dibromocyclohexane in quinoline. The oil was washed with water, dried with calcined potassium carbonate, and then heated in a round-bottomed flask to which a reflux condenser was attached. A violent reaction ensued at 170° (temperature in the flask); subsequently the contents of the flask formed two layers, though not sharply demarcated. Hydrogen bromide was copiously evolved from the reaction mixture. After completion of the violent reaction, the heating was continued and a fraction with b. p. 74-150° was collected (19.4 g). The lighter fraction was distilled off (prior to this the contents of the flask copiously evolved HBr); the distillate coming over at 74-75° was a highly refractive liquid. The amount collected up to 110° was 3.7 g. The fraction formed layers on standing. The lower layer reacted with calcined potassium carbonate with heat evolution and release of gas. After careful drying, distillation gave a fraction of 3.7 g (48.5%) with b. p. 80.5-81.5°; it crystallized at −10°; $d_4^{13.7}$ 0.8762, $n^{13.7}D$ 1.4978; McIlhinney bromine number [3] 7.72. Judging by the bromine number, the benzene content was 96%. The ultraviolet absorption spectrum of the alcoholic solution of this fraction was plotted. The character and position of the maxima are identical with those of benzene. We were more interested, however, in the spectrum of the product containing less benzene; we therefore show two curves for this material, plotted with the help of the SF-11 spectrophotometer. These relate to the product of interaction of 10.2 cyclohexane with 43 g quinoline dibromide, obtained in the final 3 g of 78.5-81° fraction, $n^{20.9}D$ 1.4711, $d_4^{20.9}$ 0.8416. Curve 1 relates to a 0.1% alcoholic solution of this product (curve 2 corresponds to the product of reaction of cyclohexene with quinoline tetrabromide).

Reaction of cyclohexene with quinoline tetrabromide. Quinoline tetrabromide was prepared by Grimaux's method [4] (slightly modified) − 12 ml bromine was added to a cooled emulsion of 15.2 g quinoline in 45 ml water. It was used without recrystallization.

20 g quinoline tetrabromide was added portionwise through a reflux condenser to 10 g freshly distilled cyclohexene. Layer formation took place: the upper layer was nearly colorless and the lower layer dark. A further 14.3 g tetrabromide was added; nearly the whole of this dissolved. The layers were separated. The upper (aqueous) layer weighed 9.3 g. When mixed with water it deposited a further small quantity of yellow oil. The lower layer (31.2 g) was transferred to a Wurtz flask and cautiously heated. Reaction commenced at 170° (temperature in the
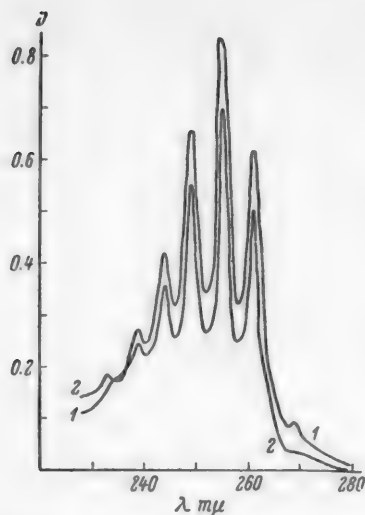
Ultraviolet absorption curves (see text for explanation).

liquid). At 142° a fairly light-colored fraction started to come over together with much hydrogen bromide. At 184° the heating was stopped. The distilled products weighed 17.6 g. The distillate was washed with dilute sulfuric acid which caused the lower (colored) layer to disappear; it was then washed with water and dried with calcium chloride and calcined potassium carbonate. From the products collected at 80.5-160° (10.2 g) was distilled a fraction with b. p. 80.2-82°; this was a strongly refracting liquid which crystallized at −5° (5.8 g or 61% on the cyclohexene taken into reaction). Bromine number (McIlhinney) 1.6. The benzene content on the basis of the bromine number was 99.2%, $n^{19.4}$D 1.5016, $d_4^{19.4}$ 0.8795. The ultraviolet absorption spectrum of the alcoholic solution of this fraction was identical with the spectrum of benzene. As in the case of interaction of cyclohexene with quinoline bromide, we show the curve not of this product (high benzene content, crystallizing on cooling) but of the product obtained (with a lower benzene content) in one of the experiments. Reaction of 10 g cyclohexene with 20 g quinoline tetrabromide gave 6.3 g of hydrocarbon fraction boiling at 78.5-82°, $n^{20.5}$D 1.4688. The ultraviolet absorption spectrum, taken with the ISP-22 spectrograph, indicated the presence of benzene (4 benzene maxima are visible on the spectrogram). From the 78.5-81° fraction was distilled a portion with b. p. 80.5-82°, $n^{21}$D 1.4667, $d_4^{21}$ 0.8377; the absorption curve of the 0.1% alcoholic solution, taken with the SF-11 spectrophotometer, is given in the diagram (curve 2).

Vacuum distillation of the heavy oil (residue from the fraction crystallizing on cooling with b. p. 80.5-82° and $n^{19.4}$D 1.5016) gave a fraction with b. p. 97-98° at 10 mm (7.8 g), $n^{19.4}$D 1.5520, M 231. Calculated for 1,2-dibromocyclohexane: M 242; for bromocyclohexene: M 159.

Interaction of cyclohexene with hexabromoethane and quinoline. 13 g freshly distilled quinoline was added to 50.3 g hexabromoethane (obtained by Gustavson's method [5]) in a flask with a reflux condenser topped by a calcium chloride tube. 8.2 g cyclohexene was run into the resulting viscous mass through a dropping funnel (strong cooling was observed during this operation). The contents of the flask were heated on an oil bath at 150-155° for 3.5 hrs. The reflux condenser was replaced by an Anschütz fitting, and a wide fraction in the 80-220° range was distilled off (30.7 g). Considerable evolution of hydrogen bromide occurred at the same time. Most of the distillate came over at 80-120°. The mass was washed with dilute sulfuric acid (the quantity of oily product was reduced by this treatment to 24 g), then with water, and dried. Subsequent distillation gave 11.5 g of slightly cloudy liquid in the 78-158° range. Fractionation at atmospheric pressure from a Favorskii flask gave a fraction with b. p. 78-83° (4.5 g or 57.5% on the cyclohexene taken into reaction). A small quantity of bromine remained in the fraction (Beilstein test) in spite of careful purification. Our determinations of the constants − $d_4^{18.2}$ 1.0253 and $n^{18.2}$D 1.4977 − also indicated the presence of a bromide; the bromine number of 7.28(McIlhinney) corresponded to a benzene content of about 97%. The product did not crystallize when cooled to −5°. The ultraviolet absorption spectrum of the alcoholic solution was taken with the ISP-22 spectrograph. The position and character of the five maxima on the spectrogram coincided with those of benzene.

## SUMMARY

1. Cyclohexene, the more saturated isolog of 1,3-cyclohexadiene, is capable like the latter of transformation into an aromatic system under the conditions of the reaction of conjugated halogenation and dehalogenation.

2. Heating of cyclohexene with quinoline polybromides (either the dibromide or the tetrabromide) as well as with hexabromoethane in presence of quinoline causes a considerable proportion to be converted to benzene (46.57, 60.51 and 55.78%, respectively).

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# INVESTIGATION OF THE EXCHANGE OF OXY RADICALS FOR THE HYDROCARBON RADICALS OF ORGANOMAGNESIUM COMPOUNDS

## IV. INTERACTION OF GRIGNARD REAGENTS WITH ORGANIC ACYLALS

### M. F. Shostakovskii and M. R. Kulibekov

In our preceding communications [1] we studied the exchange of oxy radicals of organic and organosilicon acetals for radicals of organomagnesium compounds. It was established that heavier oxy radicals are more readily replaced. In the case of organosilicon acetals the oxy radical that is usually replaced is one containing a silicon atom.

The present investigation was devoted to the interaction of a Grignard reagent with organic acylals. We know from the literature [2] that acylals are not susceptible to the symmetrization reaction, although they readily exchange their acyl group for an alkoxy radical. It was of interest to study the behavior of acylals in reactions with organomagnesium compounds. In the case of reaction of a series of organomagnesium compounds with butoxy-ethylidene acetate, we showed that the Grignard reagent initially reacts with the carbonyl group of the acylals to form a mixed acetal of a tertiary alcohol, which in turn again reacts with the organomagnesium compound and exchanges the residue of the tertiary alcohol for an organic radical according to the scheme

$$\mathrm{CH_3CH}\begin{matrix}\diagup \mathrm{OC_4H_9}\\ \diagdown \mathrm{OCOCH_3}\end{matrix} + 2\mathrm{RMgX} \rightarrow \mathrm{CH_3CH}\begin{matrix}\diagup \mathrm{OC_4H_9}\\ \diagdown \underset{\underset{\mathrm{CH_3}}{|}}{\mathrm{OC(C_4H_9)_2}}\end{matrix} \xrightarrow{+\mathrm{RMgX}} \mathrm{CH_3CH}\begin{matrix}\diagup \mathrm{OC_4H_9}\\ \diagdown \mathrm{R}\end{matrix},$$
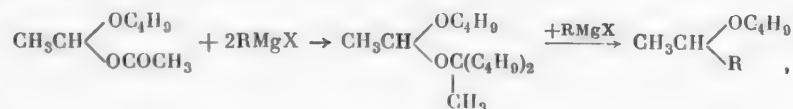
where R = H, $C_4H_9$, $C_6H_5CH_2$, $C_6H_5$; X = Cl or Br.

In addition we established that a certain proportion of the acetal undergoes symmetrization during the process with formation of two acetals:

$$2\mathrm{CH_3CH}\begin{matrix}\diagup \mathrm{OC_4H_9}\\ \diagdown \underset{\underset{\mathrm{CH_3}}{|}}{\mathrm{OC(C_4H_9)_2}}\end{matrix} \rightarrow \mathrm{CH_3CH(OC_4H_9)_2} + \mathrm{CH_3CH}\left[\underset{\underset{\mathrm{CH_3}}{|}}{\mathrm{O-C(C_4H_9)_2}}\right]_2.$$
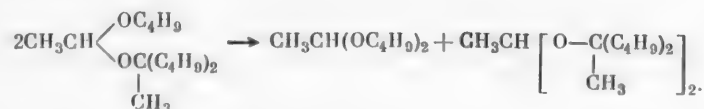
The transition from acylals to mixed acetals of tertiary alcohols and the symmetrization of the latter have not been discussed in the literature. These reactions can evidently serve for the synthesis of mixed acetals with primary and tertiary radicals.

The butyl ether of methylbenzylcarbinol synthesized by us has a delicate floral odor whose aromaticity is not inferior to that of β-phenylethyl alcohol.

### EXPERIMENTAL

1. Reaction of ethylidene acetate with butyl magnesium bromide. To the Grignard reagent prepared from 4 g magnesium and 23 g butyl bromide was added 15 g butoxyethylidene acetate at room temperature with stirring.

The mixture was then heated for 2 hrs at 35–36° and treated (with cooling) with 5% acetic acid. The ethereal layer was collected, washed with 5% sodium carbonate solution and then with water, and dried over sodium sulfate. The ether was taken off and the residue fractionated to give the following products:

4.07 g butyl ether of methylbutylcarbinol with b. p. 53–54° at 4 mm, $n^{20}D$ 1.4100, $d_4^{20}$ 0.7884, $MR_D$ 49.88, calc. 50.02.

1.61 g dibutylacetal [3] and 2.88 g mixed acetal of butyl alcohol and methyldibutylcarbinol with b. p. 79–80° at 6 mm, $n^{20}D$ 1.4156, $d_4^{20}$ 0.8200, $MR_D$ 78.89; calc. 79.39. Found %: C 74.27, 74.07; H 13.66, 13.65. $C_{16}H_{34}O_2$. Calculated %: C 74.42; H 13.18.

Also isolated were 1.56 g methyldibutylcarbinol [4] with b. p. 86–87° at 5 mm, $n^{20}D$ 1.4330, $d_4^{20}$ 0.8305; and 2.02 g symmetrical acetal of methyldibutylcarbinol with b. p. 93–95° at 5 mm, $n^{20}D$ 1.4239, $d_4^{20}$ 0.8132, $MR_D$ 107.30, calc. 107.08. Found %: C 76.81, 77.02; H 14.05, 13.95. $C_{22}H_{46}O_2$. Calculated %: C 77.19; H 13.46.

The symmetrical acetal of methyldibutylcarbinol is a transparent liquid with a pleasant odor, insoluble in water, easily soluble in organic solvents.

2. Reaction of butoxyethylidene acetate with benzyl magnesium chloride. The procedure followed the same lines as that in the preceding reaction. Starting components were 6 g magnesium, 31.6 g benzyl chloride and 15 g butoxyethylidene acetate. The following were obtained:

5.7 g butyl ether of methylbenzylcarbinol (a liquid with a pleasant floral odor) with b. p. 89–89.2° at 22 mm, $n^{20}D$ 1.4873, $d_4^{20}$ 0.9109, $MR_D$ 60.71; calc. 60.28. Found %: C 81.74, 81.64; H 10.20, 10.10. $C_{13}H_{20}O$. Calculated %: C 81.26; H 10.40.

5.75 g methyldibenzylcarbinol with b. p. 153–156° at 2.5 mm, $n^{20}D$ 1.5578, $d_4^{20}$ 1.0381, $MR_D$ 70.27; calc. 70.41. Found %: C 84.35, 84.56; H 8.25, 8.36. $C_{16}H_{18}O$. Calculated %: C 84.83; H 7.97.

3. Reaction of butoxyethylidene acetate with phenyl magnesium bromide. 12.5 g butoxyethylidene acetate was added to phenyl magnesium bromide prepared from 4 g magnesium and 26 g bromobenzene. This synthesis gave:

4.54 g methylphenylcarbinol [5] with b. p. 118–119.5° at 9 mm, $n^{20}D$ 1.4838, $d_4^{20}$ 0.9101; and 2.59 g 1,1-diphenylethylene with b. p. 127–128° at 9 mm, $n^{20}D$ 1.5968, $d_4^{20}$ 1.0326. The constants agree entirely with those reported in the literature [6].

## SUMMARY

1. The reaction of butoxyethylidene acetate with Grignard reagent was investigated. It was shown that reaction occurs at the carbonyl acyl group with formation of the corresponding mixed acetals. The mixed acetals in turn enter into exchange reaction with the Grignard reagent to form the corresponding butyl ethers.

2. The mixed acetal of butyl alcohol and methyldibutylcarbinol is susceptible to symmetrization.

3. Methyldiphenylcarbinol, formed during the exchange reaction of the corresponding mixed acetal, easily undergoes dehydration under the reaction conditions and forms 1,1-diphenylethylene.

4. The following were synthesized for the first time: mixed acetal of butyl alcohol and methyldibutylcarbinol, ditertiary acetal of methyldibutylcarbinol, methyldibenzylcarbinol, and the butyl ether of methylbenzylcarbinol.

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# SYNTHESIS AND TRANSFORMATIONS OF α-SUBSTITUTED VINYL ETHERS

## VII. SYNTHESIS AND TRANSFORMATIONS OF α-CHLOROISOPROPYL ARYL ETHERS

M. F. Shostakovskii, E. P. Gracheva, and N. K. Kul'bovskaia

In the present work we studied the synthesis of α-chloroisopropyl aryl ethers prepared by hydrochlorination of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers. Their properties were also studied. The following were prepared for the first time; α-chloroisopropyl phenyl, and the corresponding m-cresyl, guaiacyl and cyclohexyl ethers by the reaction

$$CH_2=C-OAr + HCl \longrightarrow (CH_3)_2CCl-OAr$$
$$\vert$$
$$CH_3$$
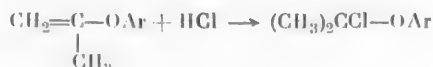
According to the literature [1], the α-chloroisopropyl alkyl ethers are extremely unstable and quickly break down to alkyl chloride and acetone. The α-chloroethers $CH_3-CHCl-OAr$, described by one of us [2], are more stable than α-chloroisopropyl aryl ethers. The latter break down when distilled; they blacken when stored for 2-3 hrs; they can be kept longer in solution in diethyl ether. α-Chloroisopropyl aryl ethers can be arranged in the following order of stability: α-chloroisopropyl phenyl > m-cresyl > guaiacyl > cyclohexyl.

Due to their instability on distillation, the prepared α-chloroisopropyl aryl ethers were characterized by various chemical reactions. Hydrogen halide and acetone were determined nearly quantitatively after hydrolysis. With excess of alcoholic alkali the expected alkyl phenyl ketal gives breakdown products — α-methylvinyl alkyl ether and phenol. Potassium phenoxide reacts to give diphenyl ketal in low yield.

α-Chloroisopropyl aryl ethers are of interest as starting substances for preparation of the little studied tert-alkyl aryl ethers.

$$(CH_3)_2C-OAr + RMgHal \longrightarrow (CH_3)_2C-OAr + MgClHal$$
$$\vert \qquad\qquad\qquad\qquad \vert$$
$$Cl \qquad\qquad\qquad\qquad\quad R$$
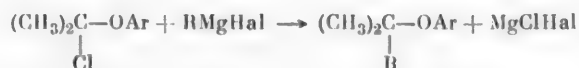
A few members of this series of ethers have been described in the literature [3]. We prepared tert-butyl phenyl, tert-amyl phenyl, 1,1-dimethylbutyl phenyl, tert-amyl m-cresyl ethers. They are colorless liquids with a pleasant odor; when boiled they rearrange to the corresponding tert-alkyl phenols [4].

## EXPERIMENTAL

The starting α-methyl-substituted vinyl ethers were prepared by the method previously described [5].

Synthesis of α-chloroisopropyl phenyl ether. 35 g α-methylvinyl phenyl ether (b. p. 61-69° at 16 mm, $n^{20}D$ 1.5048) was put into a three-necked flask fitted with thermometer, stirrer and reflux condenser (the latter topped by a calcium chloride tube). A stream of dry hydrogen chloride was introduced with stirring and cooling to −20°, the speed being so regulated that the temperature did not rise above −10°. The reaction was continued to full saturation in the couse of 3 hrs. The solution then had a brown color. (Reaction in diethyl ether gives a product with a lighter color.) Without the temperature being raised above 0°, the excess of hydrogen chloride was purged out with a stream of dry nitrogen; the increase in weight was 10.6 g (instead of 10.7). The α-chloroether

| Name of compound | Yield (%) | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. | Found (%) C | Found (%) H | Empirical formula | Calculated (%) C | Calculated (%) H |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Tert-butyl phenyl ether* | 12 | 62—63°(10) | 1.4885 | 0.9240 | 46.82 | 46.42 | — | — | $C_{10}H_{14}O$ | — | — |
| Tert-amyl phenyl ether | 40 | 104—105°(28) | 1.4910 | 0.9282 | 51.04 | 51.24 | 80.54, 80.73 | 9.88, 9.93 | $C_{11}H_{16}O$ | 80.46 | 9.82 |
| 1,1-Dimethylbutyl phenyl ether | 34 | 86—87°(6) | 1.4961 | 0.9302 | 55.97 | 55.66 | 81.40, 81.46 | 9.99, 10.07 | $C_{12}H_{18}O$ | 80.87 | 10.18 |
| Tert-amyl m-cresyl ether | 30 | 116—117°(29) | 1.4912 | 0.9191 | 55.20 | 55.66 | 80.88, 80.78 | 10.21, 10.20 | $C_{12}H_{18}O$ | 80.85 | 10.17 |

* Literature data: $n^{20}D$ 1.4880, $d_4^{20}$ 0.9247 [4]. Due to the agreement between the constants, an analysis was not performed.

was used in various reactions in the undistilled form. In similar fashion we prepared $\alpha$-chloroisopropyl m-cresyl, $\alpha$-chloroisopropyl guaiacyl and $\alpha$-chloroisopropyl cyclohexyl ethers.

Hydrolysis of $\alpha$-chloroisopropyl phenyl ether. An ampoule containing a weighed sample of the ether (0.5-0.7 g) was placed in an Erlenmeyer flask with a ground glass stopper, containing 50 ml distilled water. The ampoule was crushed, and the solution was mixed for about an hour on a shaker. The resulting acid was titrated with 0.1 N caustic alkali in presence of methyl orange [2]. Found: 97.6-98.1% of titrated hydrochloric acid. After the titration of the acid, 70 ml of 0.5 N hydroxylamine hydrochloride solution was added and the acetone content was determined. Found in the hydrolyzate: 98.5, 98.8% acetone. Similar hydrolyses were performed on $\alpha$-chloroisopropyl m-cresyl, guaiacyl and cyclohexyl ethers. Found: 98-99% of titratable hydrochloric acid and 98.5-99% acetone.

Reaction of $\alpha$-chloroisopropyl phenyl ether with butanol. A solution of sodium alkoxide, prepared by reacting 2.93 g Na with 14.82 g anhydrous butyl alcohol, was charged into a three-necked flask fitted with stirrer, thermometer, condenser and dropping funnel. Dropwise addition was made (with cooling to $-3$ to $-5°$) of 8.3 g $\alpha$-chloroisopropyl phenyl ether. The precipitate of sodium chloride (2.7 g) was filtered off and the filtrate was distilled to give 3.9 g phenol and 0.5 g $\alpha$-methylvinyl butyl ether; b. p. 113°, $n^{20}D$ 1.4118 [6].

Reaction of $\alpha$-chloroisopropyl phenyl ether with ethyl magnesium bromide. Dropwise addition of 36 g $\alpha$-chloroisopropyl phenyl ether was made to an equimolar quantity of ethyl magnesium bromide prepared from 22.9 g $C_2H_5Br$ and 5.1 g Mg in a flask equipped with condenser, stirrer and thermometer. The solution was stirred 2 hrs and left overnight. The mixture was decomposed with 10% $H_2SO_4$ in ether. The ethereal layer was collected, washed with water and caustic alkali for removal of phenolic products, dried with potassium carbonate, and distilled in vacuo. There was obtained 14.2 g of a fraction with b. p. 98-103° (28 mm), which after redistillation had b. p. 104-105° (28 mm); it was tert-amyl phenyl ether; yield 40%.

The physicochemical constants of tert-butyl phenyl, tert-amyl phenyl, 1,1-dimethylbutyl phenyl and tert-amyl m-cresyl ethers, prepared by the above procedure, are listed in the table.

## SUMMARY

1. $\alpha$-Chloroisopropyl phenyl, $\alpha$-chloroisopropyl m-cresyl, $\alpha$-chloroisopropyl guaiacyl and $\alpha$-chloroisopropyl cyclohexyl ethers were prepared. Their structure was verified by hydrolysis and by reactions with alcohols, phenols and Grignard reagent.

2. It was shown that these ethers are less stable than the corresponding $\alpha$-chloroethyl ethers.

3. Tert-butyl phenyl, tert-amyl phenyl, tert-amyl m-cresyl and 1,1-dimethylbutyl phenyl ethers (not described in the literature) were synthesized and characterized.

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* Original Russian pagination.  See C. B. translation.

# SYNTHESIS AND TRANSFORMATIONS OF α-SUBSTITUTED VINYL ETHERS

## VIII. SOME PROPERTIES OF α-METHYLVINYL ARYL AND α-METHYLVINYLCYCLOHEXYL ETHERS

M. F. Shostakovskii, E. P. Gracheva, and N. K. Kul'bovskaia

In the present work we describe the conditions for addition of alcohols and phenols to α-methylvinyl aryl ethers [1] with the objective of preparing alkyl aryl and diaryl ketals (I) and (II); we also consider the polymerization of α-methylvinyl aryl ethers by an ionic mechanism.

$$CH_2=\underset{\underset{CH_3}{|}}{C}-OAr \qquad \begin{array}{l} \xrightarrow{\text{ROH}} (CH_3)_2C\big\langle\begin{smallmatrix}OAr\\OR\end{smallmatrix} \quad (I) \\[2ex] \xrightarrow{\text{ArOH}} (CH_3)_2C\big\langle\begin{smallmatrix}OAr\\OAr\end{smallmatrix} \quad (II) \end{array}$$
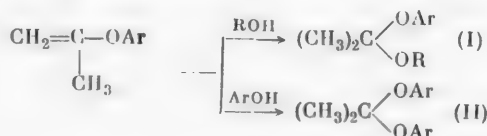
The synthesis of ketals (I, II) is not mentioned in the literature. Methods of preparation of the corresponding acetals are known [2, 3], and their properties have been studied. In particular their susceptibility to disproportionation and to ready cleavage of phenol has been demonstrated. It is interesting to note that ketals are very much more prone to disproportionate and to split off alcohols [4, 5]. This characteristic enables us to obtain α-substituted vinyl ethers starting from 2,2-dimethoxyalkanes [4]. Under similar conditions ethylidene acetals $RCH(OCH_3)_2$ do not give the corresponding unsaturated ethers.

We attempted to realize the synthesis of alkyl aryl ketals in presence of an inorganic acid (HCl) by reacting α-methylvinyl aryl ethers with alcohols. The resulting ketal (I) decomposed, however, into phenol and α-methylvinyl alkyl ether (III); the latter reacts with the alcohol to give a dialkyl ketal (IV) if excess of alcohol is used in the reaction.

$$\underset{(I)}{(CH_3)_2C\big\langle\begin{smallmatrix}OR\\OAr\end{smallmatrix}} \longrightarrow ArOH + \underset{(III)}{CH_2=\underset{\underset{CH_3}{|}}{C}-OR} \xrightarrow{\text{ROH}} \underset{(IV)}{(CH_3)_2C(OR)_2}$$
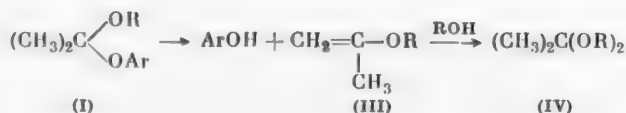
Alkyl aryl acetals likewise tend to split off phenols [3] when heated, but they can be isolated in the pure form. The tendency of alkyl aryl ketals to split off phenols is so great that mixed ketals cannot be prepared. The behavior of butyl cyclohexyl ketals illustrates the instability of mixed ketals.

Addition of phenols to α-methylvinyl aryl ethers in presence of mineral acid leads to formation of diaryl ketals (II) which have not been described in the literature. It was not possible, however, to prepare mixed diaryl ketals or symmetrical diguaiacyl and dicyclohexyl ketals.

The susceptibility of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers to polymerization was investigated. We know that polymerization of ethers by an ionic mechanism proceeds with greater facility at the boiling point of the original ethers [6], and the reaction of high-boiling ethers is effected at reduced pressure. We therefore performed the polymerization of the ethers in question in vacuo at a temperature corresponding to the boiling point of the original ether. Boron fluoride etherate was used as catalyst. Under these conditions a small

quantity of viscous polymer is formed. Elementary analysis for C, H and O indicates that polymerization goes with partial decomposition.

When polymerization of these ethers is performed in presence of boron fluoride etherate in the cold (−5°), viscous polymers are obtained whose elemental composition (C, H and O) corresponds to that of the original monomers. The yield of these low-molecular products was extremely low; their molecular weight is more than twice that of the monomer. Characteristics of the prepared polymers are given in Table 2.

We represent the mechanism of polymerization of $\alpha$-methyl aryl ethers in the first stage of the reaction in presence of ionic catalysts in the following form: $BF_3 + H_2O$ (trace) $\rightarrow$ $(BF_3 \cdot OH^-) + H^+$.

Subsequently a carbonium ion is formed under the action of the proton:

$$CH_3 \overset{+}{-}\underset{\underset{CH_3}{|}}{C} -OAr + nCH_2 = \underset{\underset{CH_3}{|}}{C} -OAr \rightarrow$$

$$\rightarrow CH_3 -\underset{\underset{CH_3}{\diagdown}}{\overset{\diagup OAr}{C}} \left[ CH_2 -\underset{\underset{CH_3}{\diagdown}}{\overset{\diagup OAr}{C}} \right]_{n-1} CH_2 -\underset{\underset{CH_3}{\diagdown}}{\overset{\diagup OAr}{C}} \cdots$$
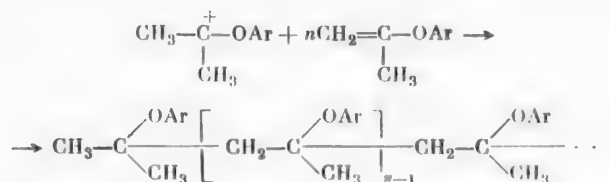
## EXPERIMENTAL

The starting $\alpha$-methylvinyl aryl ethers were synthesized by the method developed by us [7].

1. Preparation of diphenyl ketal. 18.4 g $\alpha$-methylvinyl phenyl ether and 12.9 g phenol were placed in a 100 ml 3-necked flask fitted with stirrer, thermometer and reflux condenser. After 1 drop of 33% hydrochloric acid had been introduced, the temperature rose from 20 to 93°. The mixture was left overnight. The faint-yellow solution was neutralized with anhydrous sodium carbonate, the precipitate was filtered off, and the filtrate was distilled. After a mixture of unreacted ether and phenol had come over, 12.1 g diphenyl ketal was isolated; b. p. 154-155° (12 mm).

Di-m-cresyl ketal and butyl cyclohexyl ketal were prepared by the same procedure. Results are presented in Table 1.

2. Reaction of $\alpha$-methylvinyl phenyl ether with ethyl alcohol. 20 g $\alpha$-methylvinyl phenyl ether and 7 g (slight excess) anhydrous alcohol were put into a 100 ml 3-necked flask fitted with mechanical stirrer, thermometer and reflux condenser. The mixture was well stirred, and 1-2 drops of 33% hydrochloric acid was added. The reaction temperature was observed to rise from 20 to 100°. The mixture was left overnight. The yellow solution was neutralized with anhydrous sodium carbonate, the precipitate was filtered off, and the filtrate was distilled to give the following fractions: 1st, b. p. 26-48° (30 mm), 1.9 g; 2nd, b. p. 48-53° (30 mm), 1.3 g; 3rd, b. p. 70-83° (28 mm), 1.1 g; 4th, b. p. 83-105° (26 mm), 12.9 g; 5th, b. p. 110-160° (26 mm), 2 g. The residue was 1.1 g of tarry liquid.

4.9 g of liquid was collected in a trap (after the receiver) which was immersed in a mixture of acetone and dry ice. The 1st and 2nd fractions and the trapped liquid were treated with metallic sodium in diethyl ether. Redistillation gave 1.2 g (10%) of $\alpha$-methylvinyl ethyl ether with b. p. 62-63° (754 mm), $n^{20}D$ 1.3900*; and 0.8 g diethyl ketal with b. p. 113° (754 mm), $n^{21}D$ 1.3867. 12.8 g phenol was obtained from the 3rd and 4th fractions.

3. Reaction of $\alpha$-methylvinyl guaiacyl ether with butyl alcohol. The above procedure was employed for reaction of 5 g $\alpha$-methylvinyl guaiacyl ether with 4.5 g anhydrous butyl alcohol. The following fractions were obtained: 1st, b. p. 52-58° (44 mm), 1.8 g; 2nd, b. p. 75-77° (27 mm), 3.1 g; 3rd, b. p. 105-108° (27 mm), 2.7 g. Treatment with metallic sodium in diethyl ether followed by redistillation of the 1st and 2nd fractions gave 2.5 g (36.5%) of dibutyl ketal with b. p. 94° (35 mm), $n^{20}D$ 1.4170.** The 3rd fraction gave 2.3 g guaiacol.

4. Ionic polymerization of $\alpha$-methylvinyl aryl and $\alpha$-methylvinyl cyclohexyl ethers in presence of boron fluoride etherate by boiling in vacuo [6]. A weighed quantity (5-8 g) of the ether was placed in a 3-necked flask

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* According to [8] the compound has b. p. 61-62° (752 mm), $n^{20}D$ 1.3913.
** Literature [1]: b. p. 69-70° (24 mm), $n^{20}D$ 1.4150.

TABLE 1

Physicochemical Constants of Synthesized Ketals

| Name of compound | Yield (%) | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. | Found (%) C | Found (%) H | Empirical formula | Calculated (%) C | Calculated (%) H |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Diphenyl ketal | 39 | 154—155 (12) | 1.5502 | 1.0702 | 67.94 | 67.55 | 78.88, 78.81 | 7.05, 7.04 | $C_{15}H_{16}O_2$ | 78.91 | 7.06 |
| Di-m-cresyl ketal | 20 | 175—177 (15) | 1.5423 | 1.0342 | 77.82 | 76.79 | 79.55, 79.41 | 7.59, 7.73 | $C_{17}H_{20}O_2$ | 79.64 | 7.86 |
| Butyl cyclohexyl ketal | 19 | 113—114 (15) | 1.4432 | 0.8994 | 63.19 | 63.32 | 73.58, 72.61 | 11.97, 12.13 | $C_{13}H_{26}O_2$ | 72.85 | 12.23 |

TABLE 2

Characteristics of Polymers of α-Methylvinyl Aryl Ethers

| Name of ether | Experimental conditions | Appearance | Yield (%) | Molecular weight* | Viscosity (in centipoises) | Found (%) C | Found (%) H | Empirical formula | Calculated (%) C | Calculated (%) H |
|---|---|---|---|---|---|---|---|---|---|---|
| α-Methylvinyl phenyl | Boiling in vacuo, 1 hr | Light-yellow, viscous | 36 | 299.4, 295.1 | 0.6890 | 82.40, 82.17 | 6.75, 6.95 | $C_9H_{10}O$ | 80.6 | 7.52 |
| α-Methylvinyl phenyl | Cooling at −5°, 4 hrs | Light-yellow, viscous | 57 | 278.3, 285.4 | 0.6810 | 80.71, 80.58 | 7.47, 7.64 | $C_9H_{10}O$ | 80.6 | 7.52 |
| α-Methylvinyl m-cresyl | Boiling in vacuo, 1 hr | Light-brown, viscous | 38 | 338.4, 348.7 | 0.6798 | 83.24, 83.41 | 8.91, 8.78 | $C_{10}H_{12}O$ | 81.16 | 8.14 |
| α-Methylvinyl guaiacyl | Boiling in vacuo, 1 hr | Light-brown, solid | 26 | 376.1, 360.0 | 0.6916 | 78.17, 78.04 | 8.30, 8.21 | $C_{10}H_{12}O$ | 73.25 | 7.35 |
| α-Methylvinyl guaiacyl | Cooling to −5°, 4 hrs | Light-yellow, viscous | 51 | 350.2, 342.8 | 0.6811 | 73.49, 73.35 | 7.48, 7.46 | $C_{10}H_{12}O_2$ | 73.25 | 7.35 |
| α-Methylvinyl cyclohexyl | Boiling in vacuo, 1 hr | Light-yellow, viscous | 40 | 298.1, 312.0 | 0.6847 | 79.47, 79.50 | 10.80, 10.68 | $C_9H_{16}O$ | 77.80 | 11.50 |

* Cryoscopically in benzene.

fitted with reflux condenser attached to a Vigreux column, a thermometer, and a capillary extending to the bottom of the flask. The ether was heated on an oil bath to boiling point in the vacuum of a water jet pump. Addition of 2-3 drops of a freshly prepared 12% solution of $BF_3$ etherate in diethyl ether caused a slight rise (10-25°) of temperature and darkening of the solution. After 30 min heating, the flask was cooled, and a stream of gaseous ammonia was introduced to neutralize the catalyst. The viscous solution was transferred to a flask for steam distillation. After 150 ml water had distilled over, a reddish resin was observed in the residue. The resin was separated from water and dissolved in benzene, and the benzene was driven off at 40-50 mm. The residue was brought to constant weight in a vacuum-desiccator. Results are presented in Table 2.

5. Ionic polymerization of α-methylvinyl aryl ethers in presence of boron fluoride etherate at low temperature. A weighed amount of ether (5-10 g) was placed in a 3-necked flask fitted with stirrer and thermometer. The flask was cooled to −5°. The temperature of the mass rose to +5° when a drop of 12% solution of $BF_3$ etherate in diethyl ether was added. The mixture was kept at this temperature for 3-4 hrs, after which it was brought to room temperature. After gaseous ammonia had been introduced, the polymer was worked up as described above. Results are presented in Table 2.

## SUMMARY

1. Conditions for addition of alcohols and phenols to α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers were investigated.

2. It was shown that alkyl aryl ketals are incapable of existence and easily break down with liberation of phenol.

3. The possibility of indirect preparation of α-methylvinyl alkyl ethers was demonstrated, starting from α-methylvinyl aryl ether and the appropriate alcohol (via ketals).

4. Diphenyl and di-m-cresyl ketals and butyl cyclohexyl ketal (not previously described in the literature) were prepared.

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Institute of Organic Chemistry of the Academy of
Sciences of the USSR

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* Original Russian pagination. See C. B. translation.

# SYNTHESIS AND STUDY OF N-OXIDES OF HETEROCYCLIC COMPOUNDS

## I. N-OXIDE DERIVATIVES OF MORPHINE, TETRAHYDROISOQUINOLINE AND QUINOLINE

A. M. Khaletskii, V. G. Pesin, and Chou Ts'in

Heterocyclic N-oxides have been known for a long time, but their chemistry has been inadequate studied; certain N-oxides are interesting not only biologically (iodinin, aspergillic acid, etc.) but they also possess value in the synthesis of difficultly available compounds (4-nitropyridine, etc. [1]). In this communication we present the data obtained in a study of the synthesis and properties of some N-oxide derivatives of morphine, tetrahydro-isoquinoline and quinoline.

The oxidation of codeine (I) with 3% hydrogen peroxide gave codeine N-oxide (II), m. p. 206-208° (literature [2], m. p. 230-231°); the oxidation of dihydrohydroxycodeinone (III) with 3% $H_2O_2$ in alcohol medium gave the corresponding N-oxide (IV), m. p. 152-153° (with decomp.), whose picrate had m. p. 190-192°, and whose hydrochloride had m. p. 167-168°.
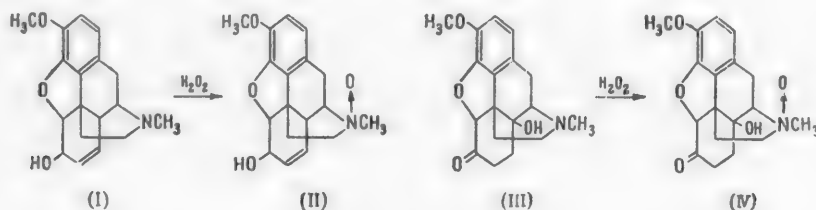


Dihydrohydroxycodeinone N-oxide (IV) reacts in a peculiar manner with sulfur dioxide; reaction of the latter with an alcoholic solution of (IV) yields a water-soluble substance (VI), m. p. 169-170°; an aqueous solution of (VI) when made alkaline with sodium hydroxide gave the original dihydrohydroxycodeinone (III) as a precipitate. Acidification of an aqueous solution of (VI), followed by the addition of barium chloride, gave a precipitate of barium sulfate. From this it could be postulated that dihydrohydroxycodeinone N-oxide (IV) reacts with sulfurous acid* to form the sulfate of dihydrohydroxycodeinone (III).

$$(IV) \xrightarrow{H_2SO_3} (III) \longrightarrow \begin{array}{l} \xrightarrow{KOH} (III) \\ \xrightarrow{HCl+BaCl_2} (III) + BaSO_4 \end{array}$$
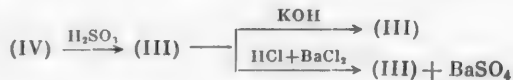
However, such a postulation is not supported experimentally. Substance (VI) melts at 169-70°, whereas the sulfate of (III) melts at 138-139°; the mixed melting point of the latter with (VI) shows a depression. In addition, based on the analysis data, the composition of substance (VI) corresponds to that of the hydrate. On the basis of the presented data it is possible to postulate that the oxidation of dihydrohydroxycodeinone (III) yields the corresponding N-oxide hydrate (V), which when reacted with sulfur dioxide is converted to a compound that is isomeric with the sulfate (VI).

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* Although the reaction was run with dry sulfur dioxide gas in anhydrous alcohol, still it could always be assumed that a trace amount of moisture (0.026 g), necessary to form sulfurous acid [based on the amount of (III) consumed], is present under the experimental conditions.
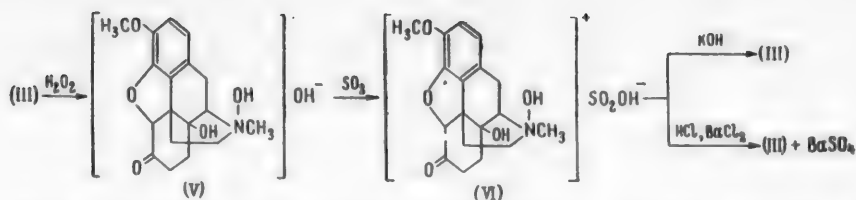
Consequently, the oxidation of (III) yields a completely substituted ammonium derivative of the type $[(R)_3NOH]^+OH^-$, where R, a hydrocarbon radical, is converted on further treatment with sulfur dioxide to sulfate (VI), by analogy with the example cited in [3].

$$[(R)_3NOH]^+OH^- + HCl \rightarrow [(R)_3NOH]^+Cl^- + H_2O$$

The oxidation of salsolidine (VII) with 3% hydrogen peroxide in aqueous acetone gave substance (VIII), m. p. 100-101°, which reduced Fehling solution and ammoniacal silver oxide solution, but which failed to give any derivatives characteristic for the aldehyde group. It is possible to assume that the substance is N-hydroxysalsolidine, having the structure of (VIII).
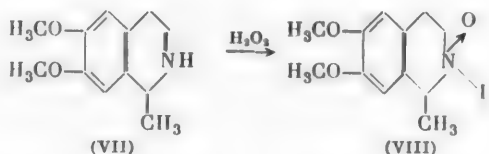


When salsoline was oxidized with either hydrogen peroxide or perbenzoic acid we were unable to isolate N-hydroxysalsolidine, which is in agreement with the literature data [4] on the lesser activity of salsoline when compared with salsolidine. The oxidation of the N-methyl derivatives of salsolidine and salsoline led to the quite easy formation of the corresponding N-oxides (IX and X).
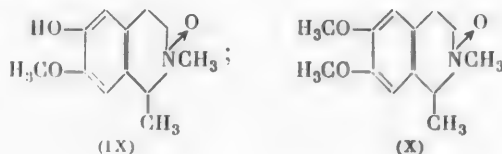


As regards the N-oxides of the 8-hydroxy- and 8-ethoxyquinolines, then judging by the literature data [5], it is possible to obtain them by the oxidation of the original quinolines with perbenzoic acid; the oxidation of 8-hydroxyquinoline with hydrogen peroxide in the presence of glacial acetic acid enabled us to obtain the corresponding N-oxide in very low yield, while the oxidation of 8-ethoxyquinoline under the indicated conditions failed to give us even traces of 8-ethoxyquinoline N-oxide. Positive results were obtained only when the 8-hydroxy- and 8-ethoxyquinolines were heated with hydrogen peroxide to 50-60° in the presence of acetic acid. As was established by us, 8-hydroxyquinoline N-oxide is formed in much smaller yield than is 8-ethoxyquinoline N-oxide, which can be explained by the influence of the hydrogen bond in the structure of 8-hydroxyquinoline. In view of the fact that 8-ethoxyquinoline N-oxide melts at 60° and even considerably lower when impure, we purified it through the picrate and the hydrochloride; the free base was isolated from the hydrochloride.

The ethylation of 8-hydroxyquinoline N-oxide with ethyl iodide gave 8-ethoxyquinoline N-oxide (XII) in 62% yield; in this respect 8-hydroxyquinoline N-oxide differs sharply from quinoline N-oxide [as is known, the methylation of the latter yields the iodide with structure (XIII)].

$$\text{(XI)} \quad \xrightarrow{\text{C}_2\text{H}_5\text{I}} \quad \text{(XII)} \qquad \text{(XIII)} \xleftarrow{\text{CH}_3\text{I}}$$

(XI)  (XII)  (XIII)
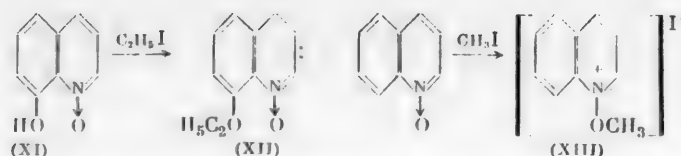
The influence of substituents on the oxidation of quinoline derivatives was also demonstrated to us in the action of peracetic acid on 2-phenylquinoline-4-carboxylic acid (atophan) (XIV), where the corresponding N-oxide (XV) was isolated in 80% yield; when the oxidation was run with an excess of 30% hydrogen peroxide in the presence of aqueous acetic acid we isolated, besides atophan N-oxide (XV), also N-benzoylanthranilic acid (XVI).

$$\text{(XIV)} \quad \xrightarrow{\text{H}_2\text{O}_2} \quad \text{(XV)} \quad + \quad \text{(XVI)}$$

(XIV)  (XV)  (XVI)
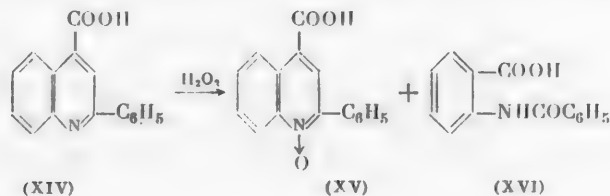
## EXPERIMENTAL

Codeine N-oxide (II).  A mixture of 45 ml of 3% hydrogen peroxide and 8.4 g of codeine (I) was heated on a water bath at 50-60°; removal of the water by vacuum-distillation gave 8 g of (II), which after recrystallization from water melted at 206-208°; white needles, soluble in water and alcohol.

Found %: N 4.37, 4.51. $C_{18}H_{21}O_4N$. Calculated %: N 4.44.

Codeine N-oxide hydrochloride.  A hot solution of 1.6 g of (II) in 5 ml of alcohol, obtained by heating on the water bath, was treated with 1 ml of hydrochloric acid (d 1.19); we obtained 1.35 g (87%) of substance with m. p. 209-214°. After recrystallization from alcohol, m. p. 214-217°.

Dihydrohydroxycodeinone N-oxide (tecodine) (IV).  A solution of 5 g of dihydrohydroxycodeinone hydrochloride in 40 ml of water was treated with 10 ml of 10% NaOH solution; after washing the precipitate with water and drying at 100° we obtained 4.15 g (93.2%) of dihydrohydroxycodeinone (III), m. p. 213-216°.

7 g of (III) was added to a mixture of 40 ml of alcohol and 30 ml of hydrogen peroxide (3%); the mixture was heated on the water bath and the solvent removed by vacuum-distillation to give 3.25 g (46.2%) of substance, m. p. 152-153° (with decomp.). Dihydrohydroxycodeinone N-oxide (IV) is a white crystalline powder, difficultly soluble in alcohol, and moderately soluble in water; it forms a red color when heated with acetic anhydride.

Found %: C 62.18, 61.51; H 6.66, 6.76; N 3.97, 3.71. $C_{18}H_{23}O_5N$. Calculated %: C 61.89; H 6.59; N 4.01.

Dihydrohydrocodeinone N-oxide picrate.  The picrate was obtained by adding a saturated solution of picric acid to an alcohol solution of dihydrohydroxycodeinone N-oxide; the precipitate after drying had m. p. 190-192.

Dihydrohydroxycodeinone N-oxide hydrochloride.  An alcohol solution of HCl was added to an alcohol solution of 0.8 g of dihydrohydroxycodeinone N-oxide; the solution was concentrated in vacuo, and after standing for 10 days, gave 0.65 g of substance, which after recrystallization from alcohol, and then from ether, melted at 167-168°. The compound was obtained as white needles, readily soluble in alcohol and in water.

Isomer of dihydrohydroxycodeinone sulfate (VI?).  Dihydrohydroxycodeinone N-oxide (IV) (0.5 g) was dissolved in anhydrous alcohol with heating, and the solution was saturated with dry sulfur dioxide, obtained by the decomposition of sodium sulfite with sulfuric acid. Evaporation of the alcohol solution gave 0.37 g (62.5%) of substance, which after recrystallization from anhydrous alcohol melted at 169-170° (with decomp.). The compound is readily soluble in water and gives a precipitate of barium sulfate when treated with barium chloride in the presence of hydrochloric acid.

Found %: C 52.23, 52.12; H 5.72, 5.58; N 3.16, 3.22; S 7.85, 7.59. $C_{18}H_{23}O_8NS$. Calculated %: C 52.23; H 5.57; N 3.16, 3.22; S 7.75.

Hydrolysis. Hydrolysis of the substance with m. p. 169-170° with 10% sodium hydroxide solution gave a precipitate, which after recrystallization from a mixture of alcohol and water had m. p. 207-209°; the mixed melting point with dihydrohydroxycodeinone was not depressed.

Dihydrohydroxycodeinone sulfate. The addition of concentrated $H_2SO_4$ to an alcohol solution of the substance with m. p. 207-209° gave a precipitate, which after recrystallization from water had m. p. 138-139°.

N-Hydroxysalsolidine (VIII). A mixture of 3 g of salsolidine (VII), 20 ml of acetone and 30 ml of water was treated with 2.5 ml of 30% hydrogen peroxide. The mixture was allowed to stand at room temperature for several days, after which the acetone was distilled off, and the aqueous solution was extracted with ether. The ether solution after drying over anhydrous sodium sulfate was distilled to remove the ether; we obtained 0.5 g (15.48%) of substance, which after recrystallization from a mixture of alcohol and water had m. p. 100-101°. The compound was obtained as a white powder, and reduced both Fehling solution and ammoniacal silver oxide solution.

Found %: C 64.65, 64.67; H 7.34, 7.44; N 6.33, 6.39. $C_{12}H_{17}O_3N$. Calculated %: C 64.57; H 7.62; N 6.28.

1,2-Dimethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline N-oxide* (N-methylsalsolidine N-oxide) (IX). A mixture of 6 g of N-methylsalsolidine, 25 ml of 95% alcohol, 25 ml of water and 3.5 ml of 30% hydrogen peroxide solution was stirred for 4 days, after which the aqueous alcohol solution was vacuum-distilled, the residual yellowish liquid dissolved in alcohol, and the alcohol solution treated with a saturated alcohol solution of picric acid. We obtained 11 g of N-methylsalsolidine N-oxide, m. p. 122-130°; after recrystallization from a mixture of alcohol and water (1 : 1), m. p. 133-134°. Reaction of the picrate of N-methylsalsolidine N-oxide with hydrochloric acid gave the hydrochloride, which was extracted with hot benzene after removal of the picric acid by filtration. The hydrochloride of N-methylsalsolidine N-oxide after purification with alcohol and ether had m. p. 162-163° (with decomp.).

Found %: C 57.32, 57.51; H 7.41, 7.57; N 5.32, 5.28. $C_{13}H_{19}O_3N \cdot HCl$. Calculated %: C 57.04; H 7.31; N 5.12.

Attempted oxidation of salsoline. a) Oxidation with hydrogen peroxide. A solution of 1 g of salsoline in 8 ml of 98% acetic acid was treated with 10 ml of 3% hydrogen peroxide; the mixture was heated on the water bath, the water was vacuum-distilled, and the residue, a thick red oily liquid, was treated with alcohol and 1 ml of hydrochloric acid. The obtained precipitate had m. p. 212° and did not give a melting point depression when mixed with authentic salsoline.

b) Oxidation with hydrogen peroxide in neutral medium. A mixture of 1 g of salsoline and 100 ml of 95% alcohol was heated on the water bath at 60°. The mixture on cooling gave a crystalline substance with m. p. 210°, which did not depress the melting point when mixed with authentic salsoline.

c) Oxidation with perbenzoic acid. A mixture of 1 g of salsoline, 80 ml of chloroform and 10 ml of alcohol was heated under reflux, and then with ice cooling the solution was treated with 70 ml of a chloroform solution containing 1.2 g of perbenzoic acid. An individual substance could not be isolated when the yellowish-brown residue was treated with 10% ammonia solution.

N-Methylsalsoline N-oxide (X). A mixture of 0.5 g of N-methylsalsoline,** 10 ml of water and 0.3 ml of 30% hydrogen peroxide was stirred for 3 days, after which the reaction mixture was vacuum-distilled at a temperature not exceeding 40°. Treatment of the residual viscous liquid with an alcohol solution of hydrogen chloride gave 0.3 g of a white precipitate with m. p. 172-174°, which after recrystallization from alcohol and ether had m. p. 186°, and was readily soluble in water. Treatment with 25% ammonia solution gave white crystals with m. p. 181-183° (with decomp.).

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* 1,2-Dimethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline was obtained by the method described in the literature [6]; its picrate had m. p. 218.
** 1,2-Dimethyl-6-hydroxy-7-methoxytetrahydroisoquinoline with m. p. 139-142° was obtained by the method described in the literature [7].

Found %: C 55.21, 55.30; H 7.20, 7.04; N 5.47, 5.38. $C_{12}H_{17}O_3N \cdot HCl$. Calculated %: C 55.50; H 6.93; N 5.39.

8-Hydroxyquinoline N-oxide (XI). a) Oxidation of 8-hydroxyquinoline with perbenzoic acid. A chloroform solution of perbenzoic acid, containing 0.512 g of active oxygen, was cooled to 1° and then 4.5 g of 8-hydroxyquinoline in 20 ml of chloroform was added gradually. The next day the chloroform was vacuum-distilled, and the viscous residue was first washed with ammonia solution by decantation, then with water, and finally recrystallized from water. The compound was obtained as yellow needles with m. p. 137-138°.

b) Oxidation of 8-hydroxyquinoline with peracetic acid. A mixture of 25 ml of 98% acetic acid, 19.2 ml of acetic anhydride and 25 ml of 30% hydrogen peroxide was heated at 40-45°, and in 3 hrs 5 g of 8-hydroxyquinoline was added gradually with constant stirring. A large amount of heat was evolved during reaction, the temperature of the solution rose to 100°, and the solution turned red. The solution was cooled to 50°, kept at this temperature for 16 hrs, the acetic acid vacuum-distilled from the reaction mixture, the residue treated with water, and the precipitate filtered. The aqueous solution was extracted 3 times with chloroform, and the chloroform solution was washed with water, dried over calcium chloride, and then evaporated on the water bath to dryness. We obtained 1.1 g (20%) of yellow needle crystals, which after recrystallization from water had m. p. 133-134°. The mixed melting point with 8-hydroxyquinoline N-oxide was not depressed.

c) Oxidation of 8-hydroxyquinoline with hydrogen peroxide. A solution of 10 g of 8-hydroxyquinoline in 50 ml of 98% acetic acid was treated with 22 ml of 30% hydrogen peroxide solution, and then the mixture was heated to the boil. After 2 hrs the solution was neutralized with ammonia solution, and the obtained precipitate was recrystallized from a mixture of alcohol and water; m. p. 74-75°. The mixed melting point with 8-hydroxyquinoline was not depressed.

8-Ethoxyquinoline N-oxide (XII). a) A mixture of 0.8 g of 8-hydroxyquinoline N-oxide and 0.3 g of potassium hydroxide was dissolved in 30 ml of alcohol, and then 1 ml of ethyl iodide was added to the solution with constant stirring. The mixture was then heated on the water bath for 1 hr at the boil, the alcohol distilled off, and the residue treated with 10% sodium hydroxide solution. The alkaline solution was extracted with ether, and the ether solution was washed with water, then dried over anhydrous sodium sulfate, and finally evaporated to dryness. The residual brownish oil was treated with alcohol, and then an alcohol solution of picric acid was added; removal of the alcohol gave the picrate, which after recrystallization from alcohol had m. p. 135-138°. The mixed melting point with the picrate of 8-ethoxyquinoline N-oxide, the latter obtained by the oxidation of 8-ethoxyquinoline with peracetic acid, was not depressed.

b) A mixture of 150 ml of 98% acetic acid, 120 ml of acetic anhydride and 138 ml of 30% hydrogen peroxide was heated with constant stirring for 3 hrs at 45-50° in a flask fitted with a reflux condenser and dropping funnel; then 30 g of 8-ethoxyquinoline, obtained by the method described in the literature [8], was added gradually (here a temperature rise to 85° was observed). Then the mixture was stirred for 16 hrs at 50°. After this most of the liquid was vacuum-distilled, 200 ml of water was added to the residue, the removal of the liquid by vacuum-distillation repeated, the residue diluted with water, the solution neutralized with 10% sodium hydroxide solution, and the resulting viscous brown oil extracted with chloroform. The chloroform solution was washed with water, dried over calcium chloride, and then stirred with 36 g of picric acid to give 49.4 g (60.77%) of 8-ethoxyquinoline N-oxide picrate. After recrystallization from ethyl alcohol, m. p. 137-138°.

8-Ethoxyquinoline N-oxide hydrochloride. 8-Ethoxyquinoline N-oxide picrate (18 g) was mixed with 45 ml of hydrochloric acid (d 1.19), and the obtained picric acid was filtered. The filtrate was extracted with hot benzene (to remove picric acid), then evaporated in vacuo at 30-40° to an oily liquid, and the latter treated with alcohol and ether. The obtained yellow needle crystals were filtered and dried in a desiccator; we obtained 3.68 g (38%) of 8-ethoxyquinoline N-oxide hydrochloride, m. p. 158°.

8-Ethoxyquinoline N-oxide. A solution of 0.97 g of 8-ethoxyquinoline N-oxide hydrochloride in 1.5 ml was treated with 4 ml of 10% sodium hydroxide solution. Since the free base failed to separate here, the solution was extracted with chloroform and after drying over calcium chloride the chloroform solution was evaporated; we obtained 0.8 g (98%) of white needle crystals with m. p. 56-58°. After recrystallization from ether, m. p. 61-62°.

Found %: C 69.34, 69.67; H 5.69, 5.76; N 7.37, 7.55. $C_{11}H_{11}O_2N$. Calculated %: C 69.84; H 5.82; N 7.40.

2-Phenylquinoline-4-carboxylic acid N-oxide (XV). A mixture of 250 ml of 98% acetic acid and 120 ml of 30% hydrogen peroxide, after heating on the boiling water bath, was treated with 20 g of 2-phenylquinoline-4-carboxylic acid (XIV), added portionwise in 1 hr and with stirring. Heating the mixture for 5 hrs on the boiling water bath gave a yellow precipitate, which after recrystallization from alcohol had m. p. 244°; yield 15.91 g (76%). The compound is readily soluble in ethyl and methyl alcohol, in chloroform, and is insoluble in water.

Found %: C 72.55, 72.27; H 4.20, 4.45; N 5.21, 5.20. $C_{16}H_{11}O_3N$. Calculated %: C 72.44; H 4.18; N 5.28.

N-Benzoylanthranilic acid (XVI). Recrystallization of the second portion of precipitate (obtained on pouring the acetic acid solution into water) gave N-benzoylanthranilic acid, which was obtained as pale yellow crystals with m. p. 170-172°; the yield was 3 g (15.78%, based on 2-phenyl-4-carboxylic acid).

Found %: C 69.51, 69.91; H 4.72, 4.74. $C_{14}H_{11}O_3N$. Calculated %: C 69.71; H 4.57.

Oxidation of 2-phenylquinoline-4-carboxylic acid with perbenzoic acid. A suspension of 1 g of atophan in 100 ml of chloroform was treated with 22 ml of a chloroform solution containing 0.84 g of perbenzoic acid. After 2 days the insoluble portion was filtered and recrystallized from alcohol, m. p. 210°. The mixed melting point with atophan was not depressed.

Oxidation of 2-phenylquinoline-4-carboxylic acid with hydrogen peroxide. 1 g of atophan in a mixture (1 : 1) of acetone and alcohol (75 ml) was oxidized with 8 ml of a 25% hydrogen peroxide solution at 50°. After removal of the solvents by vacuum-distillation the isolated precipitate had m. p. 206-208°, and failed to depress the melting point when mixed with atophan.

Reduction of 2-phenylquinoline-4-carboxylic acid N-oxide. A mixture of 0.5 g of atophan N-oxide, 1.5 g of sodium hydrosulfite, 10 ml of alcohol and 10 ml of water was heated under reflux for 3 hrs. The crystalline powder obtained on cooling was dried at 90°; we obtained 0.2 g of substance with m. p. 205-207°. The mixed melting point with atophan was not depressed.

## SUMMARY

1. The reaction of $H_2O_2$ with codeine, dihydrohydroxycodeinone, salsolidine, N-methylsalsolidine N-oxide, salsoline, N-methylsalsoline N-oxide, 8-hydroxyquinoline, 8-ethoxyquinoline and 2-phenylquinoline-4-carboxylic acid was studied, in which connection the corresponding N-oxides were isolated.

2. It was found that the reaction of dihydrohydroxycodeinone with sulfur dioxide yields a substance with m. p. 169-170° (with decomp.), which when hydrolyzed in the presence of caustic is converted to dihydrohydroxycodeinone. It was also found that the substance with m. p. 169-170° is different from the sulfate of dihydrohydroxycodeinone with m. p. 138-139°.

3. The reaction of peracetic acid with 8-hydroxyquinoline was investigated, and the N-oxide of the latter with m. p. 133-134° was isolated.

4. The reaction of perbenzoic acid with salsoline, 8-hydroxyquinoline and 2-phenylquinoline-4-carboxylic acid was investigated, in which connection only the N-oxide of 8-hydroxyquinoline was isolated.

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# CHEMISTRY OF PYRAZOLIDINE

## I. SYNTHESIS AND STUDY OF SOME MONO- AND DISUBSTITUTED DERIVATIVES OF 1,2-DIPHENYL-3,5-DIOXOPYRAZOLIDINE

A. M. Khaletskii, V. G. Pesin, and Teng Jun-Hsiang

Despite the fact that pyrazolidine has been known for a long time, the chemistry of its derivatives has received inadequate study; this is especially pertinent to compounds of the type of (I) and (II).
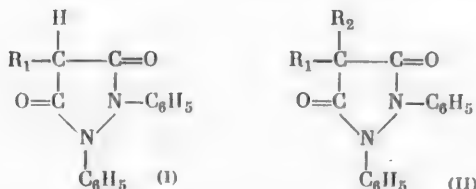


$R_1$ and $R_2$ are various radicals.

Derivatives of the (I) type can be obtained by various methods [1, 2]. We investigated the following reactions: a) reaction of 1,2-diphenyl-3,5-dioxopyrazolidine with alkyl halides, and b) reaction of an alkylmalonic ester with hydrazobenzene.
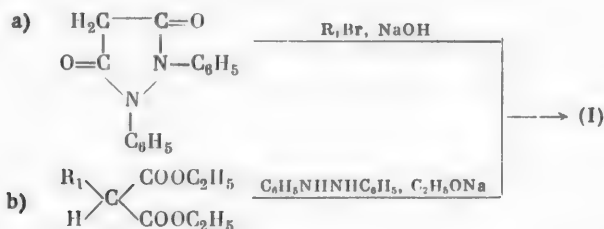


Based on the patent data [3], reaction "a" is run by reacting the starting substances at 70° in the presence of 2 N sodium hydroxide solution. When this reaction was studied by us it was found that it is impossible to isolate any noticeable amount of 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine under the indicated conditions; negative results were also obtained when the water was replaced by anhydrous alcohol. Satisfactory results were obtained when reaction "b" was studied, and here the mentioned product was isolated in 60% yield. The same method was used by us to synthesize other type (I) compounds, where R = n-$C_4H_9$, $C_6H_5$, ⬡— , $CH_3OCH_2$, $C_2H_5OCH_2$, $(CH_3)_2NCH_2-CH_2$, $(C_2H_5)_2N-CH_2-CH_2$. The synthesis of derivatives of the (II) type, where $R_1R_2$ = = $CH_3$, n-$C_4H_9$; $C_2H_5$, n-$C_4H_9$; $CH_3$, ⬡— ; $C_2H_5$, ⬡ ; was accomplished by us both by the reaction of disubstituted derivatives of malonic ester with hydrazobenzene in the presence of sodium alcoholate,

and by the reaction of 4-alkyl-1,2-diphenyl-3,5-dioxopyrazolidine with alkyl halides.

a)   $\begin{array}{c} R_1 \\ R_2 \end{array}$ C $\begin{array}{c} COOC_2H_5 \\ COOC_2H_5 \end{array}$   $\xrightarrow{C_6H_5NHNHC_6H_5, \ C_2H_5ONa}$ 

b)   (I)   $\qquad\qquad$ RBr   $\longrightarrow$ (II)
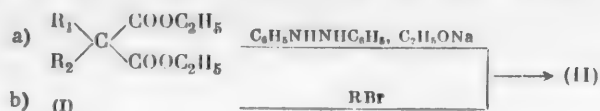
Here it was found that reaction "a" proceeds with the greater difficulty. Thus, when either $\Delta^2$-cyclohexenyl-methylmalonic ester or $\Delta^2$-cyclohexenylethylmalonic ester is reacted with hydrazobenzene in the presence of sodium alcoholate the corresponding 1,2-diphenyl-3,5-dioxopyrazolidine derivatives are formed in yields of only 2-3%. Consequently, this method does not have practical value, although the indicated reaction does have definite theoretical interest.

It is known that symmetrical disubstituted hydrazines, for example, hydrazobenzene, readily react with malonic ester but show much more difficult reaction with monosubstituted derivatives of malonic ester [2]. As regards the disubstituted derivatives, then based on literature data [4], these compounds are incapable of reacting with symmetrical disubstituted hydrazines to yield derivatives of the (II) type. As was shown by us, the alkylation of the monosubstituted derivatives of 1,2-diphenyl-3,5-dioxopyrazolidine possesses practical value (method "b"). With this method we were able to obtain the 4,4-n-butylmethyl- and 4,4-n-butylethyl-1,2-diphenyl-3,5-dioxo-pyrazolidines in 80-90% yield.

## EXPERIMENTAL

4-n-Butyl-1,2-diphenyl-3,5-dioxopyrazolidine. To a solution of 30 g of sodium metal in 1 liter of anhydrous alcohol was added, with constant stirring, 250 g of n-butylmalonic ester and 212.2 g of hydrazobenzene. The reaction was run in a 3-necked flask, fitted with a reflux condenser protected by a calcium chloride tube, and a thermometer. After boiling on the water bath until a homogeneous solution was obtained, the reflux condenser was replaced by a descending condenser, the alcohol distilled off, and the residue heated with constant stirring for 12 hrs at 130-150°. The solid mass obtained on cooling was treated with 1 liter of water, and the alkaline filtrate was extracted with ether to remove impurities, after which it was acidified until acid to Congo; the obtained yellowish oily precipitate crystallized. Recrystallization from alcohol gave 213 g of substance with m. p. 105° (60%, based on the n-butylmalonic ester), corresponding to the known 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine [3].

4-$\Delta^2$-Cyclohexenyl-1,2-diphenyl-3,5-dioxopyrazolidine. To a solution of 2.07 g of sodium metal in 45 ml of anhydrous alcohol was added with constant stirring 20 g of $\Delta^2$-cyclohexenylmalonic ester and 15.4 g of hydrazobenzene. The reaction was run under the same conditions as described for the synthesis of 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine. The precipitate obtained after acidification with hydrochloric acid was isolated, and after recrystallization from alcohol had m. p. 195-196°; yield 18 g (64%). The compound was obtained as yellow needles, insoluble in water and dilute acids, soluble in alkalies, chloroform and alcohol, and slightly soluble in ether.

Found %: C 75.97, 76.02; H 6.12, 6.17; N 8.53, 8.76. $C_{21}H_{20}O_2N_2$. Calculated %: C 75.90; H 6.02; N 8.44.

4-Dimethylaminoethyl-1,2-diphenyl-3,5-dioxopyrazolidine. To 1.25 g of sodium metal in 30 ml of anhydrous alcohol, contained in a 3-necked flask fitted with a dropping funnel and a reflux condenser protected by a calcium chloride tube, was added with constant stirring 11.5 g of ethyl dimethylaminoethylmalonate and 9.16 g of hydrazobenzene. After heating in an oil bath at 120-130°, followed by distillation of the alcohol, the residue was heated for 10 hrs at 150-160°; the reaction mass after cooling was dissolved in 200 ml of water, the solution filtered, and the filtrate neutralized with dilute hydrochloric acid. The precipitate was washed with ether and then recrystallized from alcohol to give 8 g of substance (49%) with m. p. 235-236° (with decomp.).

Found %: C 70.93, 70.69; H 7.02, 7.67; N 12.88, 12.78. $C_{19}H_{21}O_2N_3$. Calculated %: C 70.59; H 6.50; N 13.00.

The crystalline compound is insoluble in water and ether, and is soluble in dilute acids, alkalies, alcohol and chloroform.

4-Diethylaminoethyl-1,2-diphenyl-3,5-dioxopyrazolidine. The compound was obtained in the same manner as the preceding from 25 g of diethylaminoethylmalonic ester and 14 g of hydrazobenzene in the presence of 2 g of sodium metal and 50 ml of anhydrous alcohol. Yield 15.64 g (46%), m. p. 216-217°. The compound was obtained as white or slightly yellowish crystals, insoluble in water and ether, and soluble in alkalies, acids, chloroform and alcohol.

Found %: C 72.06, 72.04; H 7.53, 7.34; N 12.38, 11.97. $C_{21}H_{25}O_2N_3$. Calculated %: C 71.76; H 7.17; N 11.97.

4-Methoxymethyl-1,2-diphenyl-3,5-dioxopyrazolidine. Obtained in the same manner as the preceding from 10.2 g of methoxymethylmalonic ester and 9.2 g of hydrazobenzene in the presence of 1.4 g of sodium metal in 40 ml of alcohol. Yield 7.4 g (50%), m. p. 80-88° (with decomp.). The compound was obtained as an amorphous brownish substance, soluble in alkalies, alcohol, benzene, chloroform and ether, and insoluble in water and acids.

Found %: C 68.53, 68.41; H 5.27, 5.40; N 9.46, 9.37. $C_{17}H_{16}O_3N_2$. Calculated %: C 68.92; H 5.44; N 9.46.

4-Ethoxymethyl-1,2-diphenyl-3,5-dioxopyrazolidine. Obtained in the same manner as the preceding from 10.9 g of ethoxymethylmalonic ester, b. p. 115-120° (10 mm), and 9.2 g of hydrazobenzene in the presence of 1.4 g of sodium metal in 40 ml of anhydrous alcohol. Yield 7.8 g (50%), m. p. 55-60° (with decomp.). The compound was obtained as an amorphous substance with properties close to those of the 4-methoxy analog.

Found %: C 69.42, 69.85; H 5.62, 5.62; N 9.50, 9.75. $C_{18}H_{18}O_3N_2$. Calculated %: C 69.68; H 5.81; N 9.03.

4-Methyl-4-$\Delta^2$-cyclohexenyl-1,2-diphenyl-3,5-dioxopyrazolidine. To a solution of 3.22 g of sodium metal in 60 ml of anhydrous alcohol was added with constant stirring 32.2 g of methyl-$\Delta^2$-cyclohexenylmalonic ester and 23.18 g of hydrazobenzene. The reaction was run under the conditions described for the synthesis of 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine. Yield 1.1 g (3%), m. p. 134-136°. The compound was obtained as white crystals, insoluble in water, acids and alkalies, and soluble in ether, alcohol and chloroform.

Found %: C 76.67, 76.87; H 6.33, 6.30; N 9.34, 9.18. $C_{22}H_{22}O_2N_2$. Calculated %: C 76.30; H 6.36; N 8.09.

4-Ethyl-4-$\Delta^2$-cyclohexenyl-1,2-diphenyl-3,5-dioxopyrazolidine. Obtained in the same manner as the preceding from 30 g of ethyl-$\Delta^2$-cyclohexenylmalonic ester and 21.15 g of hydrazobenzene in the presence of 3.45 g of sodium metal and 150 ml of anhydrous alcohol. Yield 1.2 g (3%), m. p. 140-141°. The compound was obtained as white crystals, insoluble in water, acids and alkalies, and soluble in alcohol, ether and chloroform.

Found %: C 76.94, 76.72; H 6.91, 6.78; N 8.01, 7.77. $C_{23}H_{24}O_2N_2$. Calculated %: C 76.67; H 6.67; N 7.78.

4-Methyl-4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine. To a solution of 8.8 g of 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine in 200 ml of a 1% alcoholic potassium hydroxide solution was added 9 g of methyl iodide. After long standing at 20° with occasional shaking the obtained precipitate was separated, and the solution was concentrated in vacuo to remove alcohol. After adding water and ether the ether layer was separated, washed with 10% sodium hydroxide solution to remove unreacted 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine, and then with water. The ether solution was dried over anhydrous sodium sulfate, the ether removed by evaporation, and the residue recrystallized from alcohol to give 7.8 g (85%) of substance with m. p. 110-111°. The compound was obtained as white crystals, insoluble in alkalies, acids and water, and soluble in alcohol, ether and chloroform.

Found %: C 74.76, 74.46; H 6.03, 6.05; N 8.78, 8.79. $C_{20}H_{22}O_2N_2$. Calculated %: C 74.53; H 6.84; N 8.68.

4-Ethyl-4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine. A solution of 8.8 g of 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine in 200 ml of a 1% alcoholic potassium hydroxide solution was treated with 10 g of ethyl iodide, and then the reaction mixture was worked up in the same manner as the preceding; we obtained 8.2 g (87%) of substance with m. p. 72-73°. The compound was obtained as yellowish crystals, insoluble in water, alkalies and acids, and soluble in alcohol, ether and chloroform.

Found %: C 75.35, 75.00;  H 7.49, 7.14;  N 8.35, 8.72.  $C_{21}H_{24}O_2N_2$.  Calculated %:  C 75.00;  H 7.14; N 8.33.

## SUMMARY

1. The reaction of monoalkylmalonic esters with hydrazobenzene was studied, in which connection it was found that satifactory yields (< 50%) are obtained if the condensation is run in the presence of sodium metal in anhydrous alcohol medium;  this procedure was used to synthesize the following compounds: 4-n-butyl-,  4-$\Delta^2$-cyclohexenyl-, 4-dimethylaminoethyl-, 4-diethylaminoethyl-, 4-methoxymethyl- and 4-ethoxymethyl-1,2-di-phenyl-3,5-dioxopyrazolidine.  At the same time it was found, contrary to the patent data, that 4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidine is not formed in any substantial amount when the condensation of hydrazobenzene with n-butylmalonic ester is run in the presence of 2 N sodium hydroxide solution;  it is also not formed when the condensation is run in the presence of sodium hydroxide in anhydrous alcohol medium.

2. The reaction of dialkylmalonic esters with hydrazobenzene in the presence of sodium alcoholate was studied, in which connection it was shown, contrary to the literature data, that it is impossible to form dialkyl derivatives of 3,5-dioxopyrazolidine using this method.  However, we did synthesize, although in small yields ($\sim$ 3%), the 4-$\Delta^2$-cyclohexenyl-4-methyl- and 4-$\Delta^2$-cyclohexenyl-4-ethyl-3,5-dioxopyrazolidines.

3. It was shown that the alkylation of 4-monosubstituted derivatives of 1,2-diphenyl-3,5-dioxopyrazolidine with alkyl halides in the presence of 1% alcoholic potassium hydroxide solution gives the corresponding 4,4-di-substituted derivatives of 1,2-diphenyl-3,5-dioxopyrazolidine in 80-90% yields;  the 4-methyl- and 4-ethyl-4-n-butyl-1,2-diphenyl-3,5-dioxopyrazolidines were synthesized in this manner.

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# REACTION OF AMMONIA AND AMINES WITH OXIDES OF ACETYLENIC AND VINYLACETYLENIC SERIES

## NEW METHOD FOR THE PREPARATION OF PYRROLE HOMOLOGS

### F. Ia. Perveev and E. M. Kuznetsova

In a previous paper [1] we had shown that it is possible to go from $\alpha$-amino alcohols of the acetylenic and vinylacetylenic series to the corresponding pyrrole derivatives. The objective in the present study was to determine the limits of application of this new method for the preparation of pyrroles as a function of the structural traits of the oxides and amines used. In addition, we attempted to find the conditions for the one-step synthesis of pyrroles by the reaction of ammonia and amines with oxides of the acetylenic and vinylacetylenic series.

As starting products we took the oxides listed in Table 1. To develop a one-step method for the preparation of pyrrole homologs directly from the corresponding oxides via their reaction with ammonia and amines we synthesized a number of previously known compounds (XI, XVI and XVIII) (Table 2). The properties of these substituted pyrroles and their derivatives (mercury complexes, phthalides) failed to differ from the literature data. Then, by reacting oxide (II) with methylamine, benzylamine, ethanolamine and aniline we obtained pyrroles (XII-XV). To prove the structure of the simplest of the synthesized compounds (XII) we subjected it to hydrolysis in alkaline medium in the presence of hydroxylamine hydrochloride [2]. The dioxime was isolated as a result of the hydrolysis. From N-benzyl-2,4-dimethylpyrrole (XIII) we obtained the azo dye (A). The reaction of methylamine with oxide (III) gave pyrrole (XVIII) in good yield. In order to obtain the $\alpha$-phenyl-substituted pyrroles we studied the reaction of oxide (IV) with ethyl-, benzyl- and ethanolamines. The corresponding pyrroles (XIX-XXI) were isolated. A characteristic property of the $\alpha$-phenylpyrroles is their poor reactivity with mercuric chloride. The initially formed white flocculent mercury derivative rapidly assumes various bright colors on standing in the air.
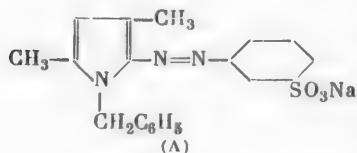
It seemed of interest to synthesize a pyrrole with a cyclohexene ring in the $\alpha$-position, since such compounds are not described in the literature, and can hardly be obtained by any other method in one step. This synthesis was accomplished by reacting ethylamine with oxide (V). The isolated pyrrole is a quite unstable liquid that polymerizes easily and suffers much tarring even when distilled under a high vacuum, leading to a sharp reduction in the yield. We were unable to isolate the completely pure product in a yield exceeding 20-25%. The mercury derivative, the same as in the case of the $\alpha$-phenyl-substituted pyrroles, is formed very slowly.

Of special interest is the synthesis of N-ethyl-4-methyl-2-vinylpyrrole (VI) and N-methyl-4-methyl-2-vinylpyrrole (VII), since a method for the preparation of such compounds has not existed up to now. An attempt to obtain vinylpyrroles by a one-step method proved unsuccessful, since the heating of oxide (I) with an excess of amine leads to closure of the pyrrole ring with the simultaneous addition of the amine to the double bond of the side chain.

**TABLE 1**

| No. | Formula | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. | Yield (In %) |
|---|---|---|---|---|---|---|---|---|
| (I) | $CH_2=CH-C\equiv C-C-CH-CH_3$ (epoxy O), $CH_3$ | 2-Methyl-1,2-epoxy-5-hexen-3-yne | 50—51° (15) | 1.4739 | 0.9149 | 33.17 | 21.3 | 70 |
| (II) | $CH_3-C\equiv C-C-CH-CH_3$ (epoxy O), $CH_3$ | 2-Methyl-1,2-epoxy-3-pentyne | 40—41 (22) | 1.4461 | 0.9264 | 22.70 | 27.60 | 75 |
| (III) | $CH_3-C\equiv C-C-CH-CH_3$ (epoxy O), $CH_3$ | 3-Methyl-2,3-epoxy-4-hexyne | 43—44 (12) | 1.4410 | 0.8856 | 32.84 | 32.56 | 75 |
| (IV) | $C_6H_5-C\equiv C-C-CH-CH_3$ (epoxy O), $CH_3$ | 2-Methyl-4-phenyl-1,2-epoxy-3-butyne | 90—92 (2) | 1.5552 | 1.0112 | 54.33 | 52.10 | 75 |
| (V) | $C_6H_9-C\equiv C-C-CH-CH_3$ (epoxy O), $CH_3$ | 2-Methyl-4-cyclohexenyl-1,2-epoxy-3-butyne | 101—102 (2) | 1.5274 | 0.9766 | 49.80 | 47.83 | 60 |
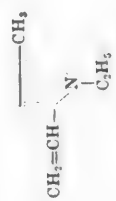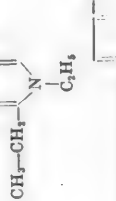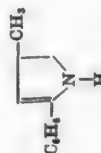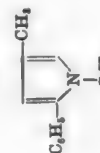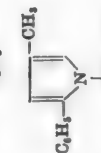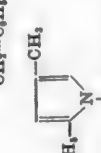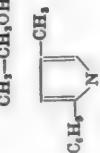
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TABLE 2

| No. | Formula | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. |
|---|---|---|---|---|---|---|---|
| (VI) | $CH_2=CH-$ ... $N-C_2H_5$, $CH_3$ | N-Ethyl-4-methyl-2-vinylpyrrole | 35—36 (1) | 1.5324 | 0.9170 | 44.20 | 45.60 |
| (VII) | $CH_2=CH-$ ... $N-CH_3$, $CH_3$ | N-Methyl-4-methyl-2-vinylpyrrole | 49 (1.5) | 1.5380 | 0.9254 | 39.76 | 40.97 |
| (VIII) | $CH_3-CH_2-$ ... $N-C_2H_5$, $CH_3$ | N-Ethyl-4-methyl-2-ethylpyrrole | 43—45 (6) | 1.4863 | 0.8852 | 44.56 | 44.46 |
| (IX) | $C_6H_5CH_2NH-CH_2-CH_2-$ ... $N-CH_2-C_6H_5$, $CH_3$ | N-Benzyl-4-methyl-2-(β-benzylaminoethyl)pyrrole | 135 (1.5) | 1.5688 | 1.0154 | 96.38 | 98.36 |
| (X) | $C_2H_5-NH-CH_2-CH_2-$ ... $N-C_2H_5$, $CH_3$ | N-Ethyl-4-methyl-2-(β-ethylamino-ethyl) pyrrole | 103—104 (0.5) | 1.4950 | 0.9162 | 57.30 | 57.15 |
| (XI) | $CH_3-$ ... $N-H$, $CH_3$ | 2,4-Dimethylpyrrole | 43 (2) | 1.4950 | 0.9208 | 30.77 | 30.16 |

TABLE 2 (continued)

| No. | Formula | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | $MR_D$ found | $MR_D$ calc. |
|---|---|---|---|---|---|---|---|
| (XII) | | N-Methyl-2,4-dimethylpyrrole | 39 (7) | 1.4831 | 0.8914 | 35.33 | 34.94 |
| (XIII) | | N-Benzyl-2,4-dimethylpyrrole | 142—145 (6) | 1.5520 | 0.9985 | 59.43 | 59.52 |
| (XIV) | | N-Ethanol-2,4-dimethylpyrrole | 83—85 (1) | 1.5067 | 1.0116 | 41.59 | 41.02 |
| (XV) | | N-Phenyl-2,4-dimethylpyrrole | 97—98 (0.5) | 1.5800 | 1.0251 | 54.82 | 55.68 |
| (XVI) | | 2,3,5-Trimethylpyrrole | 45—46 (1.5) | 1.4972 | 0.9300 | 34.22 | 34.32 |
| (XVII) | | N-Methyl-2,3,5-trimethylpyrrole | 62—64 (5) | 1.4899 | 0.9092 | 3990 | 3918 |

TABLE 2 (continued)

| No. | Formula | Name | Boiling point (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | MR$_D$ found | MR$_D$ calc. |
|---|---|---|---|---|---|---|---|
| (XVIII) |  | 4-Methyl-2-phenylpyrrole | Crystals with m. p. 151—152° | | | | |
| (XIX) |  | N-Ethyl-4-methyl-2-phenylpyrrole | 90—91 (0.5) | 1.5958 | 1.0249 | 59.44 | 61.46 |
| (XX) |  | N-Benzyl-4-methyl-2-phenylpyrrole | 151—153 (1) | 1.6151 | 1.0732 | 77.19 | 79.52 |
| (XXI) |  | N-Ethanol-4-methyl-2-phenylpyrrole | 158—160 (1) | 1.5913 | 1.0926 | 61.08 | 62.03 |
| (XXII) |  | N-Ethyl-4-methyl-2-(α-cyclohexenyl)-pyrrole | 102—105 (1) | 1.5312 | 0.9621 | 60.37 | 60.89 |
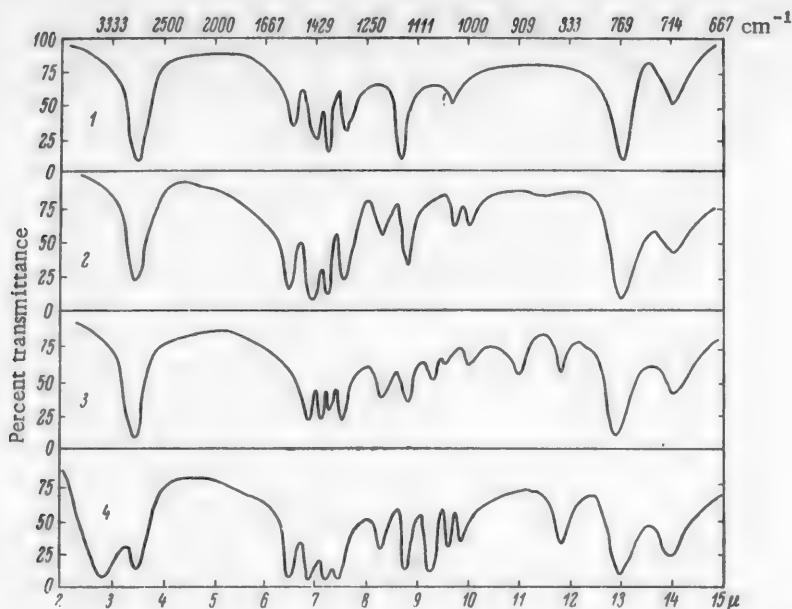
Fig. 1. Infrared absorption spectra. 1) 2,3,5-Trimethylpyrrole; 2) N-methyl-2,4-dimethylpyrrole; 3) N-ethyl-4-methyl-2-phenylpyrrole; 4) N-ethanol-2,4-di-methylpyrrole.

The reaction of ethylamine with 2-methyl-1,2-epoxy-5-hexen-3-yne gave N-ethyl-4-methyl-2-(β-ethyl-aminoethyl)-pyrrole (X). The order in which the ethylamine added to the side chain of the pyrrole was not shown conclusively. Nucleophilic substitution according to scheme (B) apparently occurs here.
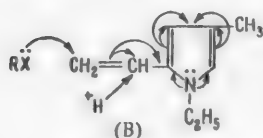


After it was established that it is possible to add ethylamine to the side chain of vinylpyrroles it seemed obligatory to determine if it is possible to add amines with heavier radicals to the vinyl group. With this in mind we studied the reaction of oxide (I) with benzylamine. Here the reaction went with the formation of large amounts of tarry products and the yield of the pure pyrrole did not exceed 25%.

To obtain N-ethyl-4-methyl-2-vinylpyrrole (VI) and N-methyl-4-methyl-2-vinylpyrrole (VII) we used the amino alcohols 1-ethylamino-2-methyl-2-hydroxy-5-hexen-3-yne and 1-methylamino-2-methyl-2-hydroxy-5-hexen-3-yne, which were obtained by the reaction of oxide (I) with ethylamine and with methylamine in the cold. The indicated alcohols were heated in sealed tubes in the presence of a small amount of quinoline. After heating for 6 hrs the corresponding pyrroles (VI and VII) were isolated, being mobile light-yellow liquids with a characteristic pyrrole.odor, insoluble in water and readible soluble in organic solvents, forming mercury derivatives, and giving a positive reaction with aqueous $SeO_2$ solution. The obtained vinyl-containing pyrroles polymerize on standing, and after several weeks are converted to a brittle glass.

To prove that a double bond is present in the side chain of N-ethyl-4-methyl-2-vinylpyrrole we subjected the compound to hydrogenation over Pt-catalyst. The amount of hydrogen absorbed corresponded to the amount theoretically required for the hydrogenation of one double bond. The product isolated from the hydrogenation was N-ethyl-4-methyl-2-ethylpyrrole (VIII), which gave characteristic pyrrole reactions with $SeO_2$ and mercuric chloride.

To prove the structure of pyrrole (VIII) we subjected it to hydrolysis in alkaline medium in the presence of hydroxylamine hydrochloride, and here the corresponding dioxime was isolated. The pyrroles synthesized by us are listed in Table 2. To prove the structure of the obtained compounds, besides chemical methods of study, we resorted to a study of the infrared absorption spectra of compounds (V–VII), (XII–XVII) and (XXIII). For this we used an IKS-11 infrared spectrometer with NaCl prism, operating in the 2-15 μ region.
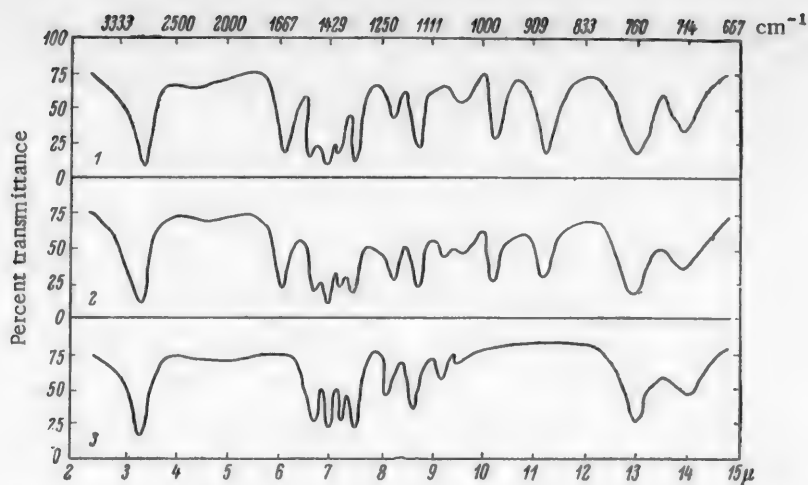
Fig. 2. Infrared absorption spectra. 1) N-Methyl-2-vinyl-4-methylpyrrole;
2) N-ethyl-2-vinyl-4-methylpyrrole; 3) N-ethyl-2-ethyl-4-methylpyrrole.
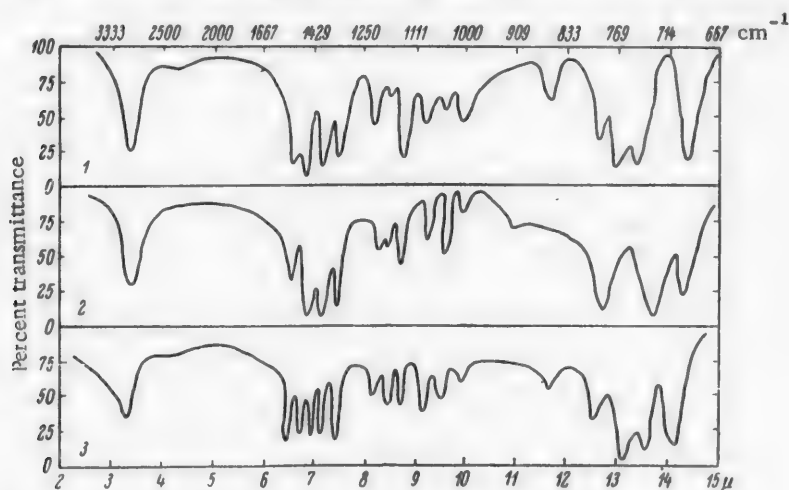


Fig. 3. Infrared absorption spectra. 1) N-Ethyl-4-methyl-2-phenylpyrrole;
2) N-benzyl-2,4-dimethylpyrrole; 3) N-benzyl-4-methyl-2-phenylpyrrole.

It was established that all of the investigated pyrroles are characterized by absorption maxima at 1530–1467, 1333 and 1144 cm$^{-1}$, corresponding to the vibration frequencies of the pyrrole ring; at 768 and 712 cm$^{-1}$, corresponding to the vibration frequencies of N—H and C—H in pyrrole; and at 2829 and 1492-1429 cm$^{-1}$, corresponding to the vibration frequencies of the $CH_2$ and $CH_3$ groups, which is in agreement with the literature data [3, 4]. In contrast to the alkyl-substituted pyrroles, the absorption spectrum of N-ethanol-2,4-dimethylpyrrole showed an absorption maximum at 3387 cm$^{-1}$, corresponding to the vibration frequency of the OH group. The absorption spectrum of N-ethyl-4-methyl-($\alpha$-cyclohexenyl)pyrrole showed an absorption band at 910 cm$^{-1}$, which apparently corresponds to the vibration frequency of C—C in the cyclohexane skeleton; the vibration frequency of the =CH bond in cyclohexene lies in the same region (Figs. 1-3).

In addition, the absorption spectra of the vinyl-substituted pyrroles showed absorption maxima at 1618 cm$^{-1}$, corresponding to the vibration frequency of the double bond in the side chain, and at 902–894 and 982 cm$^{-1}$, corresponding to the frequency of the nonplanar deformation vibration of the =C—H bond in the vinyl group.

The absorption spectrum of the hydrogenated N-ethyl-4-methyl-2-vinylpyrrole failed to show any absorption maxima characteristic for the vinyl group. The absorption spectra of the phenylpyrroles and N-benzyl-2,4-dimethylpyrrole showed absorption maxima at 710-690 and 770-730 cm$^{-1}$, corresponding to the frequencies of the nonpolar deformation vibrations of C−H in a monosubstituted benzene ring, at 1163 and 995 cm$^{-1}$, corresponding to the vibration frequencies of the benzene ring, and at 1037 cm$^{-1}$, corresponding to the vibration frequency of C−H in benzene [3, 4]. Consequently, the results of the spectroscopic studies completely confirm the chemical data obtained relative to the structure of the synthesized pyrroles.

On the basis of our study we came to the following conclusions. The reactivity of oxides of the acetylenic series depends on the nature of the substituent replacing the acetylenic hydrogen in the system

$$R-C\equiv C-\underset{\underset{R''}{|}}{C}\overset{\overset{O}{\diagup\diagdown}}{\phantom{C}}CH-R'$$
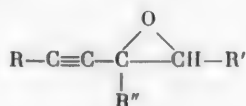
In the order of diminishing influence on the reactivity of oxides the substituents R can be arranged as follows: $CH_2 = CH > C_6H_5 >$ alkyl $>$ H.

From the literature it is known that ethylene oxide reacts with ammonia and amines much more rapidly than do its homologs, while the reactivity of oxides of the acetylenic series is somewhat greater than that of their saturated structural analogs. Thus, for example, the reaction of 2-methyl-1,2-epoxy-3-pentyne with 30% aqueous ammonia solution in the cold went to the extent of 30% in 3 days; at the same time the saturated oxide of similar structure (2-methyl-1,2-epoxypentane) reacted under the same conditions to the extent of only 10-12%.

The opening of the oxide ring is a reaction of nucleophilic substitution on the carbon, in which connection the group being replaced is the oxygen atom of the oxide [5]. The greater reactivity shown by ethylene oxide toward ammonia and amines when compared with its homologs is explained by its lack of substituents, which donate electrons to the carbon atoms of the ring. The introduction of electron-donor substituents leads to decreasing the reactivity of the oxide ring toward nucleophilic reagents (when the ring is opened under conditions of alkaline catalysis). An increased reactivity of oxides of the acetylenic series when compared with homologs of ethylene oxide is apparently due to their greater ease of polarization, which facilitates the approach of a nucleophilic reagent of the type of ammonia and amines to the reaction center.

Replacement of an alkyl radical in oxides of the acetylenic series by a vinyl group increases the polarizability of the molecule, and this explains the increase in its reactivity when compared with oxides of the acetylenic series.

The same as in the case of unsymmetrical ethylene oxide homologs, the addition of ammonia, methyl-, ethyl- and benzylamines, ethanolamine and aniline to oxides of the acetylenic and vinylacetylenic series proceeds by the Krasuskii rule, i. e., the oxide ring is opened at the most highly hydrogenated carbon atom. Proof of this is the fact that the reaction of ammonia and amines with the indicated oxides leads to the formation of pyrroles, the synthesis of which can be depicted by either scheme (B) or (C) (see diagram on following page).

Such an order for the opening of an oxide ring is explained more by the electron structure of the molecule than by steric factors. It is known that the induction effect, spreading along a chain, gradually dies out. Consequently, it is natural for the carbon atom linked to a greater number of electron-donor groups to have a higher electron density than the adjacent carbon atom. From this it is clear that attack by a nucleophilic reagent will be directed first toward the carbon atom with the smaller electron density.

If a strong electron-acceptor substituent is present on a carbon atom of the oxide ring the order in which ammonia and amines add will be the reverse of the above, and depending on the strength of the substituent, either a mixture of isomers, as in the case of styrene oxide [6], or individual products of the reverse order of substitution, as in the case of glycidic acids [5], will be formed as the result of cleavage of the oxide ring.

$$R-C\equiv C-C(OH)-CH(NHR'')-R'$$
$$|$$
$$CH_3$$

(B) $-H_2O$          (Γ)

$$\left[ R-C\equiv C-\underset{CH_3}{\overset{}{C}}=\underset{R'}{\overset{}{C}}-NHR'' \right]$$

$$\left[ \begin{array}{c} HC-C-OH \\ \; \; \; \; CH_3 \\ R-C \quad C-R' \\ N \quad H \\ R'' \end{array} \right]$$

$-H_2O$

$$\underset{R''}{\overset{CH_3}{R-\boxed{N}-R'}}$$
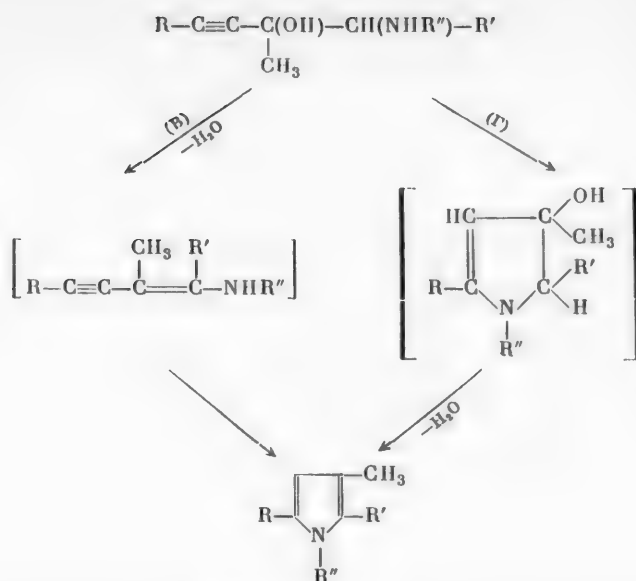
## EXPERIMENTAL

The method for the one-step preparation of pyrroles from oxides of the acetylenic series is an extremely simple one. It consists in heating the proper oxide and amine in a sealed tube on a boiling water bath, followed by separation of the water layer, and then fractional distillation of the isolated substance in vacuo (the experimental data are given in Table 3). Most of the obtained pyrroles are colorless liquids with a chloroform odor, turning yellow on storage. They give a positive test with $SeO_2$, mercuric chloride and Ehrlich reagent [7].

The mercury derivative of (XI) is white, and melts with decomposition at 135-137° (literature [8]: m. p. 136°). The mercury derivative of (XVI) had m. p. 109-110°. Long heating of (XI) with phthalic anhydride in acetic acid at 180-190° gave a crystalline yellow phthalide. M. p. 170-171° (literature [9]: m. p. 170°). The mixed melting point with authentic 2,4-dimethylpyrrole phthalide was not depressed. Substance (XI) gave a positive Ehrlich test. We also prepared the picrate of (XI) with m. p. 90.5-91.5° (literature [10]: 91-92°). Substance (XVI) did not form a picrate; also its test with Ehrlich reagent was negative. Pyrroles (XIII) and (XIV) show a slight fluorescence.

Hydrogenation of N-ethyl-4-methyl-2-vinylpyrrole. The hydrogenation was run over platinum catalyst in anhydrous alcohol solution. The amount of hydrogen consumed for 4 g of the compound was 760 ml (16.5°, 732.8 mm), or 684 ml of $H_2$ at 0° and 766 mm; the theoretical amount for the hydrogenation of one double bond is 664 ml of $H_2$. The hydrogenation product was dried over fused $K_2CO_3$, the alcohol distilled off, and the compound fractionally distilled in vacuo. We isolated 2.8 g of N-ethyl-4-methyl-2-ethylpyrrole, which gave characteristic pyrrole reactions with aqueous $SeO_2$ solution and with mercuric chloride.

Found %: N 10.15, 10.29. $C_9H_{15}N$. Calculated %: N 10.21.

Hydrolysis of N-ethyl-4-methyl-2-ethylpyrrole (VIII). A mixture of 2 g of (VIII), 2.55 g of $NH_2OH \cdot HCl$, 1.95 g of $Na_2CO_3$ and 20 g of 98% alcohol was heated for 10 hrs on the boiling water bath. The soda was filtered, and the alcohol was distilled off to a volume of 3 ml. The alcohol solution on cooling deposited a white crystalline precipitate of the dioxime, which was recrystallized from alcohol.

Found %: N 15.16, 15.10. $C_7H_{14}O_2N_2$. Calculated %: N 15.05.

Hydrolysis of N-methyl-2,4-dimethylpyrrole (XII). A mixture of 4 g of (XII), 5.1 g of $NH_2OH \cdot HCl$, 3.89 g of $Na_2CO_3$ and 40 g of 98% alcohol was heated for 11 hrs on the boiling water bath in a round-bottomed flask fitted with a reflux condenser. The soda was filtered, and then the alcohol was distilled off to a volume of 5 ml. The alcohol solution on cooling deposited a white crystalline precipitate of the dioxime, which after recrystallization from alcohol had m. p. 96-97°.

TABLE 3

| No. of ob- tained pyrrole | Amount of starting material | | Heating time (in hrs) | Yield (in %) | Empirical formula | Nitrogen content (in %) | | Amount of active H | |
|---|---|---|---|---|---|---|---|---|---|
| | oxide | amine | | | | calc. | found | calc. | found |
| (IX) | 10 g(I) | 23 g of benzyl- amine | 18 | 25 | $C_{21}H_{21}N_2$ | 9.19 | 9.04, 9.15 | — | — |
| (X) | 15 g(I) | 16 g of ethyl- amine | 6 | 68 | $C_{11}H_{20}N_2$ | 15.55 | 15.50, 15.62 | — | — |
| (XI) | 10g (II) | 25 g of 22% alcoholic ammonia solution | 10 | 59 | $C_6H_9N$ | 14.79 | 14.44, 14.65 | 1 | 0.98, 0.98 |
| (XII) | 10g (II) | 15 g of methyl- amine | 18 | 90 | $C_7H_{11}N$ | 12.82 | 12.49, 12.70 | — | — |
| (XIII) | 10g (II) | 15 g of benzyl- amine | 1 | 70 | $C_{13}H_{15}N$ | 7.56 | 7.78, 7.62 | — | — |
| (XIV) | 10 g (II) | 10 g of ethanol- amine | 15 | 70 | $C_8H_{13}ON$ | 10.06 | 10.25, 9.98 | 1 | 1.07, 1.01 |
| (XV) | 10g (II) | 20 g of aniline | 17 | 63 | $C_{12}H_{13}N$ | 8.18 | 8.30, 8.25 | — | — |
| (VI) | 14 g | 1-ethylamino- 2-methyl-2- hydroxy-5- hexen-3-yne and 1 g of quinoline | 6 | 55 | $C_9H_{13}N$ | 10.37 | 10.30, 10.40 | — | — |
| (XVI) | 10 g(III) | 27 g of 22% alcoholic ammonia solution | 9 | 64 | $C_7H_{11}N$ | 12.83 | 12.64, 12.74 | 1 | 0.97, 1.06 |
| (XVII) | 10g (III) | 5 g of methyl- amine | 9 | 62 | $C_8H_{13}N$ | 11.37 | 11.43, 11.13 | — | — |
| (XVIII) | 5 g (IV) | 20 g of 20% alcoholic ammonia solution | 10 | 50 | $C_{11}H_{11}N$ | 8.90 | 8.73, 8.75 | 1 | 1.01, 1.01 |
| (XIX) | 5g (IV) | 3 g of ethyl- amine | 10 | 70 | $C_{13}H_{15}N$ | 7.55 | 7.44, 7.61 | — | — |
| (XX) | 5g (IV) | 7 g of benzyl- amine | 10 | 75 | $C_{18}H_{17}N$ | 5.66 | 6.78, 5.58 | — | — |
| (XXI) | 7g (IV) | 5 g of ethanol- amine | 10 | 70 | $C_{13}H_{15}ON$ | 6.95 | 7.10, 6.90 | 1 | 1.02, 1.01 |
| (XXII) | 10 g (V) | 6 g of ethyl- amine | 6 | 20 | $C_{13}H_{19}N$ | 7.35 | 2.22, 7.29 | — | — |
| (XXIII) | 13 g | 1-methyl- amino-2- methyl-2- hydroxy-5- hexen-3-yne and 0.5 ml of quinoline | 6 | 75 | $C_8H_{11}N$ | 11.55 | 11.32, 11.45 | — | — |

Note.  For the structural formulas see Table 2.

Found %: N 19.61, 19.68. $C_6H_{12}O_2N_2$. Calculated %: N 19.44.

Preparation of azo dye from N-benzyl-2,4-dimethylpyrrole. The diazotization and azo-coupling were run in conventional manner (starting with 2 g of sulfanilic acid) [9]. The obtained red-yellow azo dye was recrystallized twice from water.

Found %: N 11.21, 10.85. $C_{19}H_{18}O_3N_3Na$. Calculated %: N 10.76.

## SUMMARY

1. The one-step synthesis of pyrroles by the reaction of ammonia and amines with oxides of the acetylenic and vinylacetylenic series was accomplished. The following compounds were obtained with this method: N-ethyl-4-methyl-2-vinylpyrrole, N-methyl-4-methyl-2-vinylpyrrole, N-ethyl-4-methyl-2-ethylpyrrole, N-ethyl-4-methyl-2-($\beta$-ethylaminoethyl)pyrrole, N-benzyl-4-methyl-2-($\beta$-benzylaminoethyl)pyrrole, 2,4-dimethylpyrrole, N-methyl-2,4-dimethylpyrrole, N-benzyl-2,4-dimethylpyrrole, N-ethanol-2,4-dimethylpyrrole, N-phenyl-2,4-dimethylpyrrole, 2,3,5-trimethylpyrrole, N-methyl-2,3,5-trimethylpyrrole, 4-methyl-2-phenylpyrrole, N-ethyl-4-methyl-2-phenylpyrrole, N-benzyl-4-methyl-2-phenylpyrrole, N-ethanol-4-methyl-2-phenylpyrrole, and N-ethyl-4-methyl-2-($\alpha$-cyclohexenyl)pyrrole. Of the enumerated compounds 14 are new.

2. It was established for the first time that amines readily add to the double bond found in the side chains of a vinylpyrrole.

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# TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

## XVII. ACYLATION OF BENZENE WITH THE SILICOANHYDRIDES OF ACETIC, MONO-,
## DI- AND TRICHLOROACETIC AND β-BROMOPROPIONIC ACIDS

Iu. K. Iur'ev, Z. V. Beliakova, and V. P. Volkov

Two of us had described in previous papers the use of silicoanhydrides of monobasic and dibasic organic acids as convenient acylating agents in the Gustavson-Friedel-Crafts reaction for the respective preparation of ketones [1] and keto acids [2] of the benzene, thiophene and selenophene series. In connection with this it seemed of interest to determine the possibility of acylating the benzene and thiophene nuclei with the silicoanhydrides of $\omega$-halo-substituted acids, and on the example of $\alpha$- and $\beta$-halo acids to establish the relationship between the reaction course and the position and number of halogen atoms in the acid. With this in mind we reacted silicon tetrachloride in benzene medium with acetic, mono-, di- and trichloroacetic acids, and also with $\beta$-bromopropionic acid, and used the obtained silicoanhydrides to acylate benzene in the presence of anhydrous aluminum chloride.

The acylation of benzene with the acid chlorides of mono-, di- and trichloroacetic acids, and also of $\beta$-bromopropionic acid, is described in the literature. Thus, Rothstein and Saville [3] acylated benzene with chloroacetyl chloride and obtained chloroacetophenone in 87% yield; using dichloroacetyl chloride Gautier [4] obtained dichloroacetophenone; using trichloroacetyl chloride Biltz [5] obtained trichloroacetophenone (50%). According to Delacre [6], when the last reaction is run in excess benzene the product obtained is diphenylacetophenone — the alkylation product of two molecules of benzene with trichloroacetophenone.

Foreman and McElvain [7] obtained $\beta$-bromopropiophenone in 93% yield when they acylated benzene with $\beta$-bromopropionyl chloride in carbon disulfide medium.

In seeking the optimum conditions for the acylation of benzene with tetraacyloxysilanes we improved on the method for the acylation with silicoacetic anhydride and found that the yield of acetophenone could reach 80% if the mole ratio of aluminum chloride to acid, taken to obtain the silicoanhydride, was equal to $2:1$, whereas with a $1.3:1$ ratio [8] the yield of acetophone is 47%.

In the present study we established that chloroacetic acid, reacting with silicon tetrachloride, forms silicochloroacetic anhydride, which when used to acylate benzene leads to the formation of chloroacetophenone in 45% yield when the $AlCl_3 : ClCH_2$ ratio $= 2:1$, and a 34% yield when the ratio $= 1:1$.

When benzene was acylated with silicodichloroacetic anhydride we obtained $\omega,\omega$-dichloroacetophenone in 25% yield.

$$4Cl_2CHCOOH + SiCl_4 \xrightarrow{C_6H_6} Si(OCOCHCl_2)_4 + 4HCl$$
$$4C_6H_6 + Si(OCOCHCl_2)_4 \xrightarrow{AlCl_3} 4C_6H_5COCHCl_2 + Si(OH)_4$$
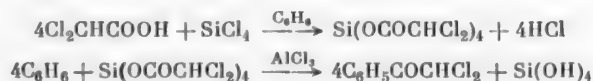
When benzene was acylated with silicotrichloroacetic anhydride we obtained, instead of the expected trichloroacetophenone or diphenylacetophenone, a small amount of p-benzhydryldiphenyl. It is possible to explain the formation of the latter by the alkylation of benzene with silicotrichloroacetic anhydride, which led to the formation of the silicoanhydride of triphenylacetic acid. One of the benzene rings of the triphenylacetic silico-

anhydride formed in this manner then condenses (under the influence of aluminum chloride) with benzene, giving the silicoanhydride of biphenyldiphenylacetic acid, which on hydrolysis gives the acid itself. The biphenyldiphenylacetic acid suffers decarboxylation when distilled, and this yields p-benzhydryldiphenyl.

$$4CCl_3COOH + SiCl_4 \longrightarrow Si(OCOCCl_3)_4 + 4HCl$$

$$Si(OCOCCl_3)_4 \xrightarrow[C_6H_6]{AlCl_3} Si[OCOC(C_6H_5)_3]_4 \xrightarrow[C_6H_6]{AlCl_3} Si\left[ OCOC\begin{matrix} C_6H_5 \\ -C_6H_4-C_6H_5 \\ C_6H_5 \end{matrix} \right]_4 \xrightarrow{4H_2O}$$

$$\longrightarrow 4C_6H_5C_6H_4-\underset{\underset{C_6H_5}{|}}{\overset{\overset{C_6H_5}{|}}{C}}-COOH \xrightarrow{-CO_2} 4C_6H_5C_6H_4-\underset{C_6H_5}{\overset{C_6H_5}{CH}}$$
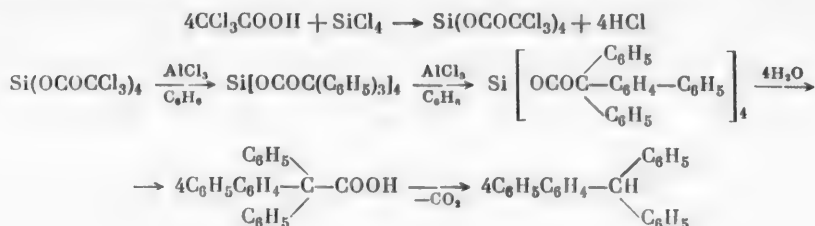
We determined the extent to which the silicoanhydrides of the chloroacetic acids were formed by the amount of hydrogen chloride evolved, and found that in benzene medium they are formed in nearly quantitative yield.

Consequently, the results obtained in the acylation of benzene with the silicoanhydrides of acetic, mono-, di- and trichloroacetic acids permit stating the following rule as regards their behavior in the Gustavson-Friedel-Crafts reaction: the stronger the acid contained in the silicoanhydride, the greater is the stability of the latter and the weaker is its acylating capacity.

This rule is also supported by the fact that the acylation of thiophene with silicochloroacetic anhydride, which we attempted to run in the presence of anhydrous stannic chloride, did not go at all, whereas when the acylation was run with silicoacetic anhydride under the same conditions we obtained acetothienone in 94% yield [1].

The acylation of benzene with the silicoanhydride of $\beta$-bromopropionic acid, using a molar ratio of $AlCl_3$: $: BrCH_2CH_2COOH = 2:1$, gave higher yields of the reaction products, reaching 90%. However, even when the reaction mass was decomposed with a mixture of ice and concentrated hydrochloric acid we obtained only $\beta$-hydroxypropiophenone (57%), being the hydrolysis product of the $\beta$-bromopropiophenone formed in the reaction, and $\beta$-phenylpropiophenone (33%), the latter being the product of the alkylation of benzene with the $\beta$-bromopropiophenone formed during the reaction

$$4C_6H_6 + Si(OCOCH_2CH_2Br)_4 \xrightarrow[C_6H_6]{AlCl_3} 4C_6H_5COCH_2CH_2Br + Si(OH)_4$$

$$C_6H_5COCH_2CH_2Br \xrightarrow[-HBr]{H_2O} C_6H_5COCH_2CH_2OH$$

$$C_6H_5COCH_2CH_2Br + C_6H_6 \xrightarrow{AlCl_3} C_6H_5COCH_2CH_2C_6H_5 + HBr$$
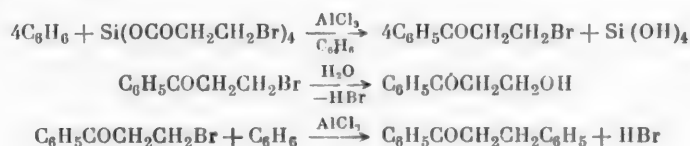
When the above reaction was run under the same conditions, but with the $AlCl_3$: $BrCH_2CH_2COOH$ ratio = $1:1$, we obtained $\beta$-bromopropiophenone in 70% yield.

When the acylation was run in nitrobenzene medium we obtained only $\beta$-hydroxypropiophenone (34%).

In the distillation of $\beta$-hydroxypropiophenone there occurred not only cleavage of water with the formation of vinyl phenyl ketone [9], but also polymerization with the formation of a crystalline substance, which proved to be a dimer in which two molecules of $\beta$-hydroxypropiophenone are apparently connected to each other through two hydrogen bonds.

$$2C_6H_5COCH_2CH_2OH \longrightarrow \begin{matrix} C_6H_5-\overset{\overset{\displaystyle \cdot}{\|}}{\underset{\displaystyle O}{C}}-CH_2-CH_2-OH \\ \vdots \quad\quad\quad\quad \vdots \\ HO-CH_2-CH_2-\underset{\displaystyle O}{\overset{\|}{C}}-C_6H_5 \end{matrix}$$
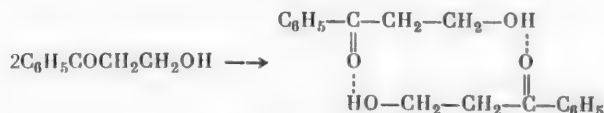
## EXPERIMENTAL

Acylation of benzene with silicoacetic anhydride. Silicoacetic anhydride was obtained by the general method, described earlier [1], from 6 g (0.1 mole) of acetic acid and 5 g (0.03 mole) of silicon tetrachloride in 150

ml of dry benzene. Then 26.7 g (0.2 mole) of anhydrous aluminum chloride was added in 20 min at 20° and the mixture heated for 5 hrs on the water bath, with gradual elevation of the temperature (the last 30 min on a boiling water bath). The mixture was cooled and poured with stirring over 250 g of ice. The benzene was steam-distilled, while the acetophenone was distilled with superheated steam. After separating the benzene layer the water layer was extracted with ether. The extracts were combined and dried over calcium chloride. After distilling off the ether and benzene the residue was distilled. We obtained 9.7 g (80%) of acetophenone: b. p. 71-72° (7 mm); m. p. 19.5-20°.

Literature data: m. p. 20° [10].

Acylation of benzene with silicochloroacetic anhydride. When 9.5 g (0.1 mole) of chloroacetic acid was reacted with 5 g (0.03 mole) of silicon tetrachloride in 150 ml of dry benzene the amount of hydrogen chloride evolved was 3.5 g (0.095 mole or 95%). Then 26.7 g (0.2 mole) of anhydrous aluminum chloride was added in small portions over a period of 3 hrs at 20°, and the mixture heated as indicated above. The chloroacetophenone after distillation with superheated steam was extracted with benzene and dried over calcium chloride. After distilling off the benzene the residue was distilled. We obtained 7 g (45%) of chloroacetophenone with b. p. 101.5-102.5° (5 mm) and m. p. 57-57.5° (from alcohol). Semicarbazone: m. p. 155-156° (from alcohol).

With a mole ratio of $AlCl_3 : ClCH_2COOH = 1:1$, the reaction of 19 g of chloroacetic acid and 10 g of silicon tetrachloride in 250 ml of dry benzene with 29.5 g of aluminum chloride gave 10.5 g (34%) of chloroacetophenone with m. p. 57-57.5° (from alcohol).

Both of the above preparations when mixed with authentic chloroacetophenone failed to depress the melting point.

Literature data: m. p. 57-58° [11]; m. p. 56° [12]. Semicarbazone: m. p. 156° [13].

Acylation of benzene with silicodichloroacetic anhydride. This acylation was run in the same manner as the acylation with silicoacetic anhydride. The reaction of 12. 9 g (0.1 mole) of dichloroacetic acid with 5 g (0.03 mole) of silicon tetrachloride in 150 ml of dry benzene resulted in the evolution of 3.62 g (99%) of hydrogen chloride. Then 26.7 g (0.2 mole) of anhydrous aluminum chloride was added, the mixture heated as already described, the reaction mass decomposed with ice and concentrated hydrochloric acid, then filtered (suction-filtration through cotton cloth), and the reaction products isolated (by distillation) from the benzene solution and the ether extract of the precipitate. We obtained: a) 5.9 g (46%) of dichloroacetic acid, and b) 4.75 g (25%) of $\omega,\omega$-dichloroacetophenone.

B. p. 80-82° (2 mm), $n^{20}D$ 1.5618, $d_4^{20}$ 1.3392, $MR_D$ 45.78. $C_8H_6OCl_2F_3$. Calculated 45.29. Found %: Cl 37.55, 37.29. $C_8H_6OCl_2$. Calculated %: Cl 37.50. Literature·data [4]: b. p. 143° (25 mm), $d^{16}$ 1.340.

With a mole ratio of $AlCl_3 : Cl_2CHCOOH = 1:1$, the reaction of 12.9 g of dichloroacetic acid and 5 g of silicon tetrachloride in 150 ml of dry benzene with 15 g (0.11 mole) of aluminum chloride gave: a) 6.5 g (50%) of dichloroacetic acid, and b) 4.6 g (24.0%) of $\omega,\omega$-dichloroacetophenone with b. p. 80-82° (2 mm), and $n^{20}D$ 1.5618.

The acylation of benzene with silicotrichloroacetic anhydride was run in the same manner as already described for acylation with silicoacetic anhydride. The reaction of 16.4 g (0.1 mole) of trichloroacetic acid with 5 g (0.03 mole) of silicon tetrachloride in 150 ml of dry benzene resulted in the evolution of 3.3 g (90%) of hydrogen chloride. Then 15 g (0.11 mole) of anhydrous aluminum chloride was added, the mixture heated as usual, the reaction mass decomposed with ice and concentrated hydrochloric acid, then filtered (suction-filtration through cotton cloth), and the reaction products isolated (by distillation) from the benzene solution and the ether extract of the precipitate. We obtained: a) 7.36 g (45.0%) of trichloroacetic acid, and b) 1.6 g (5%) of p-benzylhydryl-diphenyl with m. p. 113-114° (from alcohol).

Found %: C 93.67, 93.58; H 6.39, 6.44. $C_{25}H_{20}$. Calculated %: C 93.71; H 6.29. Literature data [14]: m. p. 112-113°.

The residue in the distillation flask was treated with caustic solution, filtered, and the filtrate extracted with ether. The alkaline solution was acidified, and the obtained precipitate, being biphenyldiphenylacetic acid (0.1 g), was filtered. The compound had m. p. 218-220°. Literature data [15]: m. p. 220-222°.

Acylation of benzene with the silicoanhydride of β-bromopropionic acid. 1) The synthesis was run in the same manner as in the acylation with silicoacetic anhydride. For reaction we took 150 ml of dry benzene, 15.3 g (0.1 mole) of β-bromopropionic acid, 5 g (0.03 mole) of silicon tetrachloride and 26.7 g (0.2 mole) of anhydrous aluminum chloride. The reaction mass after decomposition with ice and concentrated hydrochloric acid was filtered (suction-filtration through cotton cloth), and the reaction products were isolated (by distillation) from the benzene solution and the ether extract of the precipitate.

We obtained: a) 6.9 g (33%) of β-phenylpropiophenone: b. p. 154-156° (4 mm); m. p. 71.5-72°.

Found %: C 85.84, 86.07; H 6.77, 6.86. $C_{15}H_{14}O$. Calculated %: C 85.71; H 6.67.

The semicarbazone of β-phenylpropiophenone had m. p. 143-143.5° (from alcohol).

Found %: N 16.00, 16.03. $C_{16}H_{17}ON_3$. Calculated %: N 15.72.

The 2,4-dinitrophenylhydrazone of β-phenylpropiophenone had m. p. 182-183° (from ethyl acetate).

Found %: N 14.28, 14.33. $C_{21}H_{18}O_4N_4$. Calculated %: N 14.35. Literature data: m. p. 72-73° [16]; semicarbazone: m. p. 143° [17]; 2,4-dinitrophenylhydrazone: m. p. 166° [18].

b) We also obtained 8.55 g (57%) of β-hydroxypropiophenone.

B. p. 120-124° (4 mm), $n^{20}D$ 1.5365, $d_4^{20}$ 1.1078, $MR_D$ 42.31. $C_9H_{10}O_2$ $F_3$. Calculated: 41.69. Literature data: b. p. 143-144° (20 mm) [9], $n^{20}D$ 1.5332, $d_4^{20}$ 1.0983, $MR_D$ 42.43 [19].

Water was cleaved when β-hydroxypropiophenone was reacted with semicarbazide [9] and vinyl phenyl ketone was formed, as a result of which the corresponding semicarbazone was obtained with m. p. 227-227.5° (with decomp.) (from butyl alcohol).

Found %: C 63.16, 63.01; H 5.82, 5.77; N 21.74, 21.89. $C_{10}H_{11}ON_3$. Calculated %: C 63.46; H 5.86; N 22.20.

Redistillation of the β-hydroxypropiophenone also resulted in the cleavage of water and the resulting substance (b. p. 88-89° at 9 mm) when reacted with bromine in carbon disulfide gave a dibromide with m. p. 57-57.5° (from petroleum ether), being α,β-dibromoethyl phenyl ketone.

Found %: Cr 54.69, 54.59. $C_9H_8OBr_2$. Calculated %: Br 54.74. Literature data: vinyl phenyl ketone, b. p. 111-112° [9]; dibromide, m. p. 53.5-54° [20]; m. p. 58° [21].

The major portion of the β-hydroxypropiophenone formed a dimer, which was obtained as white crystals with m. p. 48.5-49° (from petroleum ether).

Found %: C 71.62, 71.63; H 6.88, 6.97. M 297, 308 (cryoscopically in benzene). $C_{18}H_{20}O_4$. Calculated %: C 71.96; H 6.71. M 300.

2) For reaction we took 150 ml of dry benzene, 20 g (0.13 mole) of β-bromopropionic acid, 7.5 g (0.04 mole) of silicon tetrachloride and 20 g (0.15 mole) of anhydrous aluminum chloride. We obtained 19.5 g (70%) of β-bromopropiophenone with m. p. 59-60° (from petroleum ether).

Found %: Br 37.43. $C_9H_9OBr$. Calculated %: Br 37.55. Literature data: m. p. 59-60° [22]; m. p. 58-59° [7].

3) From 15.3 g of β-bromopropionic acid, 5 g of silicon tetrachloride and 7.8 g of dry benzene in 150 ml of dry nitrobenzene, in the presence of 26.7 g of aluminum chloride, we obtained 5 g (34%) of β-hydroxypropiophenone: b. p. 128-133° (12 mm), $n^{20}D$ 1.5359.

## SUMMARY

1. Based on the acylation of benzene with the silicoanhydrides of acetic, chloroacetic, dichloroacetic and trichloroacetic acids in the presence of anhydrous aluminum chloride it was established that the stronger the acid forming the silicoanhydride, the greater the stability of the latter and the weaker its acylating capacity.

2. The acylation of benzene with silico-β-bromopropionic anhydride gave β-bromopropiophenone in good yield.

3. When the acylation of benzene with silico-$\beta$-bromopropionic anhydride is run under certain conditions the mobility of the halogen atom in the formed $\beta$-bromopropiophenone leads, on the one hand, to alkylation of the benzene ring by the $\beta$-bromopropiophenone, and on the other hand, to easy hydrolysis during decomposition of the complex, as a result of which the reaction products prove to be $\beta$-phenylpropiophenone and $\beta$-hydroxypropiophenone.

4. $\beta$-Hydroxypropiophenone when distilled forms a dimer with the composition $C_{18}H_{20}O_4$.

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# ETHYLENE SULFIDE IN THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS WITH TWO HETERO ATOMS

## VIII. SYNTHESIS OF 2-(2-FURYL)-, 2-(2-THIENYL)-, AND 2-(2-SELENIENYL)-3-ARYLTHIAZOLIDINES

### Iu. K. Iur'ev and S. V. Diatlovitskaia

In previous papers [1-3] we have shown that the condensation of N-($\beta$-mercaptoethyl)-arylamines with aldehydes leads to the formation of 2-alkyl- (or aryl)-3-arylthiazolidines. Since the reaction with benzaldehyde goes easily, then it could be expected that other aldehydes of an aromatic character, as for example, furfural, 2-thiophenecarboxaldehyde and 2-selenophenecarboxaldehyde, would condense with N-($\beta$-mercaptoethyl)-aryl-amines to form the corresponding thiazolidines.

From the literature it is known that S. V. Tsukerman [4] attempted to condense cysteine hydrochloride with furfural. However, the formation of 2-(2-furyl)-thiazolidine failed to occur here: only the furfural mercaptal was obtained when the reaction was run in alcohol medium, while in aqueous medium the substance obtained was free of sulfur.

In the present paper we condensed furfural, 2-thiophenecarboxaldehyde and 2-selenophenecarboxaldehyde with N-($\beta$-mercaptoethyl)-arylamines and obtained the corresponding series of thiazolidines: 2-(2-furyl)-2-arylthia-zolidines, 2-(2-thienyl)-3-arylthiazolidines and 2-(2-selenienyl)-3-arylthiazolidines.



$$Ar = C_6H_5; p- \ \& \ o\text{-}CH_3C_6H_4; \ p- \ \& o\text{-}CH_3OC_6H_4.$$
$$X = O, \ S, \ Se.$$
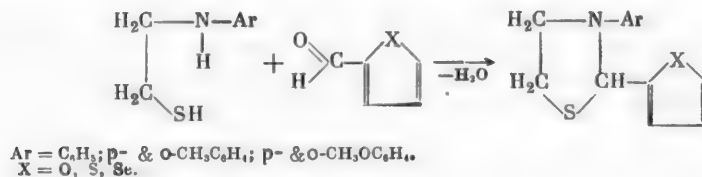
It should be mentioned that the 2-(2-furyl)-3-arylthiazolidines are quite unstable compounds: they are easily decomposed when vacuum-distilled, and also when treated with concentrated hydrochloric acid or hydrogen chloride, which makes it impossible to obtain their hydrochlorides. 2-(2-Furyl)-3-o-anisylthiazolidine proved to be so unstable that we were unable to obtain it in the pure state or to characterize it. It is probable that the instability of this type of compound was the reason for the failure of the above described attempts to synthesize 2-(2-furyl)-thiazolidine [4].

The 2-(2-thienyl)- and 2-(2-selenienyl)-3-arylthiazolidines proved to be more stable compounds: they are decomposed only when boiled with concentrated hydrochloric acid for 10-15 min.

The reactivity of the ortho-benzene-substituted isomers of the N-($\beta$-mercaptoethyl)-arylamines in the above-described reactions was poorer than that of the corresponding para-isomers, which is in agreement with earlier made observations [2, 5, 6]. Thus, when N-($\beta$-mercaptoethyl)-o-toluidine and N-($\beta$-mercaptoethyl)-o-anisidine were condensed with furfural, 2-thiophenecarboxaldehyde and 2-selenophenecarboxaldehyde the yields of the thiazolidines were lower than the yields of the corresponding thiazolidines, obtained using N-($\beta$-mercaptoethyl)-p-toluidine and N-($\beta$-mercaptoethyl)-p-anisidine in the condensation.

## Reaction of N-(β-Mercaptoethyl)-arylamines with Furfural

2-(2-Furyl)-3-phenylthiazolidine. A mixture of 7.65 g (0.05 mole) of N-(β-mercaptoethyl)-aniline and 4.8 g (0.05 mole) of furfural was boiled in 30 ml of dry benzene in a Dean-Stark apparatus until water ceased to come over in the distillate. The amount of water collected was 0.85 ml. After distilling off the benzene the oily residue was shaken with 5 ml of alcohol and 25 ml of saturated sodium bisulfite solution. The precipitate of bisulfite derivative was filtered and washed with ether. The filtrate was extracted 3 times with ether, and the combined ether extracts were dried over anhydrous magnesium sulfate.

After removal of the ether by distillation the oily residue was vacuum-distilled in a stream of nitrogen (slight decomposition). After distilling off several drops of a crimson-colored liquid the fraction with b. p. 175-180° (3 mm) was collected. This fraction, weighing 8 g (69%), was 2-(2-furyl)-3-phenylthiazolidine, and after redistillation had the following constants.

B. p. 175-176° (3 mm), $n^{20}D$ 1.6280, $d_4^{20}$ 1.2167, $MR_D$ 67.47. $C_{13}H_{13}ONS$ $F_5$. Calculated 66.85. Found %: C 66.90, 66.88; H 5.80, 5.68; N 6.03, 6.04. $C_{13}H_{13}ONS$. Calculated %: C 67.50; H 5.67; N 6.06.

2-(2-Furyl)-3-p-tolylthiazolidine. A mixture of 8.35 g (0.05 mole) of N-(β-mercaptoethyl)-p-toluidine and 4.8 g (0.05 mole) of furfural was allowed to stand at room temperature for 4 hrs, and then worked up in the same manner as described above. After distilling off the ether from the ether extract of the reaction product the residue crystallized and was 2-(2-furyl)-3-p-tolylthiazolidine: m. p. 56.5-57.5° (from alcohol). Yield 9.4 g (76.5%).

Found %: C 68.68, 68.50; H 6.12, 6.30; N 5.66, 5.76. $C_{14}H_{15}ONS$. Calculated %: C 68.54; H 6.16; N 5.71.

2-(2-Furyl)-3-p-anisylthiazolidine. From 9.15 g (0.05 mole) of N-(β-mercaptoethyl)-p-anisidine and 4.8 g (0.05 mole) of furfural, using the procedure of the preceding experiment, we obtained 11.7 g (86.5%) of 2-(2-furyl)-3-p-anisylthiazolidine: m. p. 75.5-76° (from alcohol).

Found %: C 64.52, 64.39; H 5.89, 5.87; N 5.38, 5.43. $C_{14}H_{15}O_2NS$. Calculated %: C 64.34; H 5.79; N 5.36.

2-(2-Furyl)-3-o-tolylthiazolidine. A mixture of 8.35 g (0.05 mole) of N-(β-mercaptoethyl)-o-toluidine and 4.8 g (0.05 mole) of furfural was allowed to stand for 6 hrs, and then worked up as described above. The oil, obtained after distilling off the ether, was vacuum-distilled in a stream of nitrogen, and here the following fractions were collected: 1st, b. p. 135-145° (4 mm), 1.3 g; 2nd, b. p. 145-174° (4 mm), 2.42 g; 3rd, b. p. 174-180° (4 mm), 3.8 g.

The 1st fraction was unreacted N-(β-mercaptoethyl)-o-toluidine; the 2nd fraction was a mixture of the unreacted amine and 2-(2-furyl)-3-o-tolylthiazolidine; the 3rd fraction was 2-(2-furyl)-3-o-tolylthiazolidine.

Redistillation of the 2nd and 3rd fractions gave 5.1 g (41%) of 2-(2-furyl)-3-o-tolylthiazolidine.

B. p. 180-182° (4 mm), $n^{20}D$ 1.6032, $d_4^{20}$ 1.1800, $MR_D$ 71.43. $C_{14}H_{15}ONS$ $F_5$. Calculated 71.47. Found %: C 68.61, 68.74; H 6.24, 6.26; N 6.07. $C_{14}H_{15}ONS$. Calculated %: C 68.54; H 6.16; N 5.71.

## Reaction of N-(β-Mercaptoethyl)-arylamines with 2-Thiophenecarboxaldehyde

A mixture of 0.01 g mole of N-(β-mercaptoethyl)-arylamine and 0.01 g mole of 2-thiophenecarboxaldehyde was allowed to stand at room temperature for 20 hrs. [In the case of N-(β-mercaptoethyl)-o-toluidine and N-(β-mercaptoethyl)-p-carbethoxyaniline the mixtures were allowed to stand for 40 hrs.]

The crystals of 2-(2-thienyl)-3-arylthiazolidine were filtered and recrystallized from 80% alcohol.

The constants of the 2-(2-thienyl)-3-arylthiazolidines obtained in the indicated manner are listed in Table 1.

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[*] Student G. P. Aleksandrova assisted in the experimental portion of this study.

TABLE 1

2-(2-Thienyl)-3-arylthiazolidines

| Name of obtained compounds | Melting point | Yield | | Analysis data | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | in g | in % | C | | H | | N | |
| | | | | found | calc. | found | calc. | found | calc. |
| 2-(2-Thienyl)-3-phenylthiazolidine | 70.5—71° | 2.0 | 80 | 63.42, 63.34 | 63.11 | 5.45, 5.41 | 5.30 | 5.78, 5.89 | 5.66 |
| 2-(2-Thienyl)-3-o-tolylthiazolidine | 34.5—35 | 0.53 | 20 | 64.34, 64.29 | 64.32 | 5.96, 5.91 | 5.78 | 5.31, 5.39 | 5.36 |
| 2-(2-Thienyl)-3-p-tolylthiazolidine | 72.5—73 | 2.6 | 100 | 64.17, 64.14 | 64.32 | 5.81, 5.91 | 5.78 | 5.51, 5.67 | 5.36 |
| 2-(2-Thienyl)-3-o-anisylthiazolidine | 74.5—75 | 1.7 | 61.5 | 61.04, 60.87 | 60.61 | 5.69, 5.69 | 5.45 | 5.28, 5.05 | 5.05 |
| 2-(2-Thienyl)-3-p-anisylthiazolidine | 77—77.5 | 2.75 | 100 | 60.67, 60.51 | 60.61 | 5.56, 5.61 | 5.45 | 5.30, 5.15 | 5.05 |
| 2-(2-Thienyl)-3-p-carbethoxyphenyl-thiazolidine | 105.5—106 | 1.53 | 48 | 59.94, 60.04 | 60.15 | 5.23, 5.34 | 5.36 | 4.50, 4.48 | 4.39 |

## Reaction of N-(β-Mercaptoethyl)-arylamines with 2-Selenophenecarboxaldehyde

Mixtures of 0.01 mole of N-(β-mercaptoethyl)-arylamine and 0.01 mole of 2-selenophenecarboxalde-hyde were allowed to stand for 20 hrs.

In the case of N-(β-mercaptoethyl)-p-toluidine and N-(β-mercaptoethyl)-o-anisidine the mixtures were allowed to stand for 48 hrs, after which the reaction products were dissolved in ether, and the solutions dried over anhydrous magnesium sulfate; after distilling off the ether the residues crystallized.

The crystals of 2-(2-selenienyl)-3-arylthiazolidine were filtered and recrystallized from 80% alcohol.

The constants of the 2-(2-selenienyl)-3-arylthiazolidines obtained in the indicated manner are listed in Table 2.

TABLE 2

2-(2-Selenienyl)-3-arylthiazolidines

| Name of obtained compounds | Melting point | Yield | | Analysis data | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | in g | in % | C | | H | | N | |
| | | | | found | calc. | found | calc. | found | calc. |
| 2-(2-Selenienyl)-3-phenylthiazolidine | 65.5—66° | 1.54 | 52.5 | 53.33, 53.37 | 53.06 | 4.68, 4.59 | 4.45 | 4.98, 4.92 | 4.75 |
| 2-(2-Selenienyl)-3-o-tolylthiazolidine | 56—56.5 | 1.67 | 54 | 54.68, 54.58 | 54.54 | 5.13, 5.15 | 4.91 | 4.80, 4.63 | 4.54 |
| 2-(2-Selenienyl)-3-p-tolylthiazolidine | 81.5—82 | 1.9 | 61 | 54.24, 54.43 | 54.54 | 5.07, 5.09 | 4.91 | 4.85, 4.64 | 4.54 |
| 2-(2-Selenienyl)-3-o-anisylthiazolidine | 96.5—97 | 1.73 | 52.5 | 51.70, 51.91 | 51.85 | 4.77, 4.69 | 4.66 | 4.55, 4.49 | 4.32 |
| 2-(2-Selenienyl)-3-p-anisylthiazolidine | 81—81.5 | 2.95 | 91 | 51.68, 51.71 | 51.85 | 4.85, 4.93 | 4.66 | 4.45, 4.39 | 4.32 |

## SUMMARY

1. The condensation of N-(β-mercaptoethyl)-arylamines with furfural gave the previously unknown 2-(2-furyl)-3-phenyl-, 2-(2-furyl)-3-o-tolyl-, 2-(2-furyl)-3-p-tolyl- and 2-(2-furyl)-3-p-anisylthiazolidines.

2. The condensation of N-(β-mercaptoethyl)-arylamines with 2-thiophenecarboxaldehyde gave the previously unknown 2-(2-thienyl)-3-phenyl-, 2-(2-thienyl)-3-o-tolyl-, 2-(2-thienyl)-3-p-tolyl-, 2-(thienyl)-3-o-anisyl-, 2-(2-thienyl)-3-p-anisyl- and 2-(2-thienyl)-3-p-carbethoxyphenylthiazolidines.

3. The condensation of N-(β-mercaptoethyl)-arylamines with 2-selenophenecarboxaldehyde gave the previously unknown 2-(2-selenienyl)-3-phenyl-, 2-(2-selenienyl)-3-o-tolyl-, 2-(2-selenienyl)-3-p-tolyl-, 2-(2-selenienyl)-3-o-anisyl- and 2-(2-selenienyl)-3-p-anisylthiazolidines.

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# CONDENSATION OF $\gamma$, $\gamma$, $\gamma$-TRICHLOROCROTONONITRILE WITH BENZENE IN THE PRESENCE OF ALUMINUM CHLORIDE

## A. D. Grebeniuk and I. P. Tsukervanik

In studying the influence exerted by the stability of the intermediate complex with aluminum chloride on the reactivity of $\alpha$,$\beta$-unsaturated nitriles it was shown by us [1] that $\gamma$,$\gamma$,$\gamma$-trichlorocrotononitrile reacts readily with benzene in the presence of 1.2 g-moles of $AlCl_3$. The high reactivity of this nitrile when compared with that of acrylonitrile was explained by us as being due to the influence exerted by the trichloromethyl group, which reduces the stability of the intermediate complex. As a result of reaction we obtained a 63% yield of phenyldichlorovinylacetonitrile, proved by saponification to phenylsuccinic acid. The position of the phenyl group was not determined, since on the basis of some literature data [2, 3] we assumed that the manner in which benzene adds to the double bond will be determined by the conjugation effect of the double bond with the nitrile group. Proceeding from these considerations, the reaction product was assigned the structure of $\beta$-phenyldichlorovinylacetonitrile (I).

Recently A. N. Nesmeianov, L. I. Zakharkin and R. Kh. Friedlina [4], studying the effect of $\sigma$, $\pi$-conjugation in unsaturated compounds containing a trichloromethyl group, showed that the condensation of $\gamma$,$\gamma$,$\gamma$-trichlorocrotonic acid with benzene in the presence of aluminum chloride leads to the formation of $\alpha$-phenyldichlorovinylacetic acid.

$$CCl_3CH=CH-COOH + C_6H_6 \xrightarrow{AlCl_3} CCl_2=CH-\underset{\underset{C_6H_5}{|}}{CH}-COOH$$
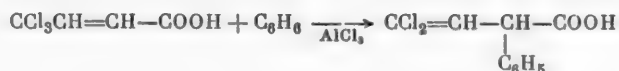
This new information, testifying to the great power exerted by the conjugation of a $CCl_3$ group with a double bond, made it necessary to determine the position of the phenyl group in the product obtained by us when $\gamma$,$\gamma$,$\gamma$-trichlorocrotononitrile was condensed with benzene.

Depending on whether the trichloromethyl or the phenyl group exerts predominant influence on the double bond it is possible to obtain either $\alpha$-phenyldichlorovinylacetonitrile (II) or $\beta$-phenyldichlorovinylacetonitrile (I), according to the scheme

$$CCl_3-CH=CH-CN \xrightarrow[AlCl_3]{+C_6H_6} \begin{cases} CCl_2=\underset{\underset{C_6H_5}{|}}{C}-CH_2-CN & \text{(I)} \\ \\ CCl_2=CH-\underset{\underset{C_6H_5}{|}}{CH}-CN & \text{(II)} \end{cases}$$
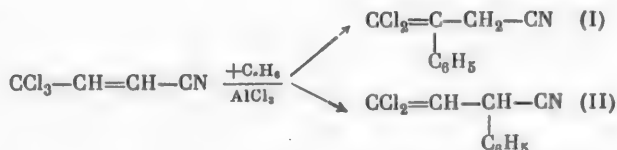
Together with a study of the condensation product, we made a more detailed study of the influence of reaction conditions on the condensation course. We were able to show that the reaction also goes in the absence of excess catalyst, using only 0.8-0.9 g-mole of $AlCl_3$. This again testifies to the high reactivity shown by $\gamma$,$\gamma$,$\gamma$-trichlorocrotononitrile. However, reducing the amount of catalyst leads to a sharp reduction in the reaction rate: if at 60-70° and a reaction time of 2-4 hrs the yield of phenyldichlorovinylacetonitrile using 1.2 g-moles of $AlCl_3$ is 62-63%, then with 0.8 g-mole of catalyst the yield of product drops to 23%, despite the fact that the reaction time is increased to 16 hrs.

Further it was established that the main reaction product, boiling in the range 130-132° at 6 mm, and 140-145° at 8 mm, is not homogeneous. Instead it consists of a mixture of two nitriles — one a liquid and the other being crystalline with m. p. 92-92.5°. The amount of either nitrile in the mixture depends on the reaction conditions. The relative amount of the crystalline nitrile increases with decrease in the amount of $AlCl_3$.

The liquid nitrile is $\alpha$-phenyldichlorovinylacetonitrile (II). Its structure was proved in the following manner: the nitrile was saponified with a mixture of hydrochloric and acetic acids to $\alpha$-phenyldichlorovinylacetic acid (III), which by hydrogenation over palladium was converted to $\alpha$-phenylbutyric acid (IV), identified by the mixed melting point of its amide with the amide of $\alpha$-phenylbutyric acid, obtained by a counter synthesis.

$$CCl_2{=}CH{-}\underset{\underset{(II)}{\overset{|}{C_6H_5}}}{CH}{-}CN \xrightarrow[CH_3COOH]{HCl} CCl_2{=}CH{-}\underset{\underset{(III)}{\overset{|}{C_6H_5}}}{CH}{-}COOH \xrightarrow[Pd,BaSO_4]{H_2}$$

$$\rightarrow CH_3{-}CH_2{-}\underset{\underset{(IV)}{\overset{|}{C_6H_5}}}{CH}{-}COOH \xrightarrow{SOCl_2} CH_3{-}CH_2{-}\underset{\overset{|}{C_6H_5}}{CH}{-}COCl \xrightarrow{NH_3}$$

$$\rightarrow CH_3{-}CH_2{-}\underset{\underset{(V)}{\overset{|}{C_6H_5}}}{CH}{-}CONH_2$$
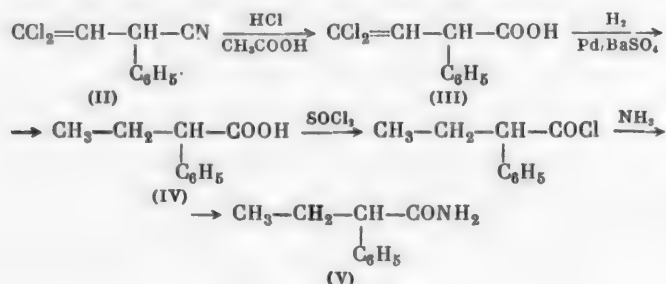
Based on its complete analysis the crystalline condensation product is an isomer of nitrile (II). When nitrile (II), containing the crystalline nitrile as impurity, was saponified, the crystalline product was recovered unchanged. From this it was concluded that it is saponified with greater difficulty. For this reason the hydrolysis of the crystalline nitrile was run with a larger amount of mixed hydrochloric and acetic acids, and for a longer time. Under these conditions both the chlorine and cyanide groups were saponified and the hydrolysis product proved to be phenylsuccinic acid.

$$CCl_2{=}\underset{\overset{|}{C_6H_5}}{C}{-}CH_2{-}CN \xrightarrow[CH_3COOH]{HCl} HOOC{-}\underset{\overset{|}{C_6H_5}}{CH}{-}CH_2{-}COOH$$

The formation of phenylsuccinic acid indicates that the crystalline nitrile differs from the $\alpha$-isomer only in the position of the phenyl group, and consequently is $\beta$-phenyldichlorovinylacetonitrile (I). To prove conclusively the structure of (I) we are synthesizing it by a counter method.

## EXPERIMENTAL

The condensation of $\gamma,\gamma,\gamma$-trichlorocrotononitrile with benzene was run in the same manner as described earlier [1]. The results are summarized in the table.

| Expt. no. | Relative amounts of reactants (g-mole) | | Temperature | Reaction time (in hrs) | | Yields of products (in % of theoretical) | |
|---|---|---|---|---|---|---|---|
| | $AlCl_3$ | $C_6H_6$ | | heating | standing at 20° | liquid nitrile (II) | crystalline nitrile (I) |
| 1 | 1.17 | 25.7 | 45° | 5 | 12 | 27 | Not isolated |
| 2 | 1.80 | 25.7 | 20 | | 22 | 24 | Traces |
| 3 | 1.00 | 10.0 | 60—70 | 10.5 | 12 | 43 | Not isolated |
| 4 | 0.94 | 13.6 | 60—70 | 12.5 | 36 | 31 | 9.6 |
| 5 | 0.80 | 13.6 | 60—75 | 15 | 84 | 11.5 | 11.5 |
| 6 | 1.20 | 10.0 | 65—70 | 6 | 12 | 44.3 | 9.7 |
| 7 | 1.20 | 10.0 | 70 | 2 | — | 62 | Not isolated |

<u>α-Phenyldichlorovinylacetonitrile (II)</u>:

B. p. 122° at 3 mm, 125-127° at 5 mm, 140-145° at 8 mm, $n^{20}D$ 1.5585, $d_4^{20}$ 1.2553, $MR_D$ 54.48; calc. 53.86.

The analysis results for (II) and its complete saponification to phenylsuccinic acid were presented earlier [1].

<u>α-Phenyldichlorovinylacetic acid (III)</u>. A mixture of 7.75 g of nitrile (II), 9 ml of concentrated hydrochloric acid, 16 ml of glacial acetic acid and 4 ml of water was refluxed for 17 hrs, and then allowed to stand at room temperature for 48 hrs. When the mixture was cooled the top brownish layer solidified, while the aqueous layer deposited white crystals. We obtained 7.5 g of crude product.

To isolate the pure acid a benzene solution of the saponification product was chromatographed through a column containing $Al_2O_3$. All of the colored impurities were eluted with benzene until the $Al_2O_3$ layer became white. The aluminum oxide with tenaciously adsorbed acid was pushed out of the column and then treated several times with 10% $NaHCO_3$ solution until all of the acid had been extracted. Acidification of the alkaline solution gave the nearly pure acid with m. p. 83-86°. After recrystallization from either cyclohexane or petroleum ether, m. p. 88-89°. From the literature, m. p. 87-88° [4].

Two substances were isolated from the benzene solution used to elute the column. One of them was orange in color, had m. p. 196-198° (from benzene), and was insoluble in ether and dilute NaOH solution. It contained both halogen and nitrogen.

The second substance with m. p. 90-91.5° proved to be nitrile (I). Its mixed melting point with nitrile (I), isolated from the condensation product, was not depressed.

<u>α-Phenylbutyric acid (IV)</u>. A solution of 2 g of acid (III) in 30 ml of water containing 1.4 g of NaOH was hydrogenated over $Pd/BaSO_4$ at room temperature. Here 625 ml of $H_2$ was absorbed. At the end of hydrogenation the catalyst was suction-filtered, and the alkaline solution after evaporation was acidified. The acid was extracted with ether, dried, and vacuum-distilled. We obtained 1.1 g of acid (IV) with b. p. 160-170° (6 mm).

<u>α-Phenylbutyramide (V)</u>. A mixture of 1.1 g of acid (IV) and 5 ml of $SOCl_2$ was refluxed for an hour. After distilling off the excess $SOCl_2$ in vacuo the crude chloride was converted to the amide by treatment with 25% ammonia solution. We obtained 0.6 g of amide (V) with m. p. 83-84.5° (from benzene), which failed to depress the melting point when mixed with the α-phenylbutyramide obtained by us from benzyl cyanide by the scheme

$$C_6H_5CH_2CN \xrightarrow[Na]{C_2H_5I} C_6H_5-CH-CN \xrightarrow[H_2O_2]{NaOH} C_6H_5-CH-CONH_2.$$
$$\underset{C_2H_5}{|} \qquad \underset{C_2H_5}{|}$$
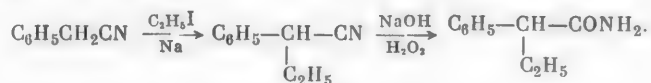
The ethylation of benzyl cyanide was run by the Wegler method [5]. To saponify the nitrile we used the method repeatedly employed by us earlier [1].

<u>β-Phenyldichlorovinylacetonitrile (I)</u>. The product, isolated from several condensations (Table, Nos. 4-6), represents a single substance, crystallizing from benzene as coarse, colorless, well-shaped crystals with m. p. 92-92.5°. It is insoluble in petroleum ether, moderately soluble in diethyl ether, and has a sharp odor reminiscent of chlorine.

Found %: C 56.83; H 3.34; Cl 34.02; N 6.88. $C_{10}H_7NCl_2$. Calculated %: C 56.60; H 3.30; Cl 33.49; N 6.60.

<u>Saponification of nitrile (I)</u>. A mixture of 1 g of nitrile (I), 4 ml of glacial acetic acid, 2 ml of concentrated HCl and 0.5 ml of water was refluxed with mechanical stirring for 13 hrs (and then allowed to stand at room temperature for 60 hrs). On pouring into water a brown oil separated that solidified on standing. The obtained substance proved to be insoluble in 10% soda solution, while the residue from the evaporation of the acid solution yielded only a trace amount of acid, which could not be purified.

The substance was again dissolved in 10 ml of $CH_3COOH$ and refluxed with 8 ml of HCl for 19 hrs (the mixture was allowed to stand for 96 hrs). A small amount of the water-insoluble substance was removed and washed with 10% soda solution. No indication of solution was observed here. The acid solution was carefully

evaporated on the water bath to a small volume. On cooling a precipitate of phenylsuccinic acid was obtained, which was reprecipitated from soda solution. We obtained 0.2 g of the acid. M. P. 164-165° (from a mixture of benzene and anhydrous alcohol). The mixed melting point with authentic phenylsuccinic acid was not depressed.

## SUMMARY

1. $\gamma$,$\gamma$,$\gamma$-Trichlorocrotononitrile adds benzene at the double bond in the presence of 0.8-0.9 g-mole of $AlCl_3$, which indicates its high activity.

2. The reaction product is a mixture of $\alpha$-phenyldichlorovinylacetonitrile and, apparently, $\beta$-phenyldichlorovinylacetonitrile. The relative amount of the two isomers in the mixture depends on the reaction conditions.

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* Original Russian pagination. See C. B. translation.

# CATALYTIC AMINATION OF ORGANIC COMPOUNDS

## VII. CATALYTIC TRANSFORMATIONS IN THE BUTYLAMINE SERIES

### N. S. Kozlov and N. I. Panova

In studying the catalytic amination of alcohols and of aliphatic ethers and esters [1-3] it was established by us that in all cases the end reaction products are a mixture of the corresponding primary, secondary and tertiary amines. Consequently, in order to elucidate the mechanism of the amination reactions taking place here the need arose to investigate the behavior shown by various individual amines under our studied conditions.

Some light on this problem was found in the patent literature. Thus, it is known that the passage of a mixture of butylamine and ammonia over aluminum oxide heated to 350° gave a catalyzate that contained 60% of unchanged butylamine, 34% of dibutylamine, 3% of butylene and 3% of other products [4]. If the aluminum oxide had been previously treated with acid, then here the yield of secondary amine showed a slight increase [5, 6].

A paper was recently published by A. F. Plate and co-workers [7], in which experiments on the conversion of propylamine to a mixture of primary, secondary and tertiary amines by passage over aluminomolybdenum catalyst are described.

In the present paper we studied the catalytic transformations of butylamine, dibutylamine and tributylamine when passed in a stream of compressed ammonia over heated aluminum oxide. Here it was established that any of the indicated starting amines give butylene and two new amines: the primary amine gives the secondary and tertiary amines, the secondary amine gives the primary, and tertiary amines and the tertiary amine gives the primary and secondary amines. The mutual transformations of the amines can be depicted by the following general equation:

$$6C_4H_9NH_2 \rightleftarrows 3(C_4H_9)_2NH + 3NH_3 \rightleftarrows 2(C_4H_9)_3N + 4NH_3$$
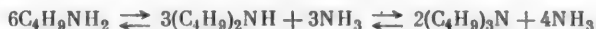
Consequently, the experimental data obtained by us indicate that the mutual transformations of the butylamines bear an equilibrium character, in which connection the equilibrium is shifted strongly toward the formation of the primary amine.

The formation of butylene in these reactions can occur as the result of the following chemical processes:

$$C_4H_9NH_2 = C_4H_8 + NH_3,$$
$$(C_4H_9)_2NH = C_4H_8 + C_4H_9NH_2,$$
$$(C_4H_9)_3N = C_4H_8 + (C_4H_9)_2NH.$$
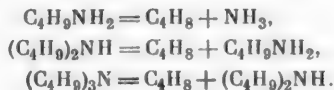
At the present time we lack experimental data showing that butylene participates in the formation of the amines. However, using compressed ammonia, we were largely able to suppress the conversion of the primary butylamine to butylene. We also made an attempt to study the reverse reaction, where as the starting ethylenic hydrocarbon we took amylene with b. p. 33°, obtained by the dehydration of isoamyl alcohol. From 10 ml of amylene taken for reaction we obtained several drops of the amine. Using the micro technique it was shown that the obtained amine has a primary character and distills completely up to 150°.

Such a reaction character is probably explained as follows: here, apparently, ammonia adds to the double bond in accord with the V. V. Markovnikov rule, in which case a primary amine is formed with the amino group on the secondary carbon atom. But amines having such a structure, as was shown in our previous paper [2], are extremely unstable.

## EXPERIMENTAL

The experiments were run in the same apparatus used by us earlier [1]. A known weight of starting amine in an atmosphere of ammonia under a pressure of 9 atmos. was passed at a rate of 20 drops per min over aluminum oxide heated to 370-375°. The amines taken for experiment had the following constants: n-butylamine, b. p. 77-79°, $d_4^{20}$ 0.743, $n^{20}D$ 1.403; di-n-butylamine, b. p. 158-160°, $d_4^{20}$ 0.767, $n^{20}D$ 1.423; and tri-n-butylamine, b. p. 214-218°, $d_4^{20}$ 0.774, $n^{20}D$ 1.425.

The gaseous reaction product proved to be butylene, which was determined by the method described in the previous paper [2]. The liquid catalyzate, boiling in the range 75-180° independent of the amine taken was a mixture of primary, secondary and tertiary amines, and did not contain any neutral products. The catalyzate was analyzed by the method given in [8].

The results of our experiments are summarized in the table.

| Name of compound | Am't of compound (in g) | Ammonia pressure (atmos) | Yield of catalyzate (in g) | Properties of catalyzate | | Am't of amines in catalyzate | | | Am't. of butylene (in liters) |
|---|---|---|---|---|---|---|---|---|---|
| | | | | primary | secondary | primary | secondary | tertiary | |
| n-Butylamine | 30 | 9 | 25 | 0.743 | 1.408 | 52.6 | 32.3 | 15.1 | 2 |
| Dibutylamine | 30 | 9 | 22 | 0.771 | 1.411 | 57.0 | 20.5 | 22.5 | 3 |
| Tributylamine | 13 | 9 | 9 | 0.763 | 1.416 | 52.8 | 22.2 | 25.0 | 1 |
| n-Butylamine | 10 | 1 | 4 | — | — | — | — | — | 4 |

## SUMMARY

The mutual transformations of butyl-, dibutyl- and tributylamine over aluminum oxide in an ammonia atmosphere under variable pressure were studied. Compressed ammonia shifts the equilibrium toward the formation of the primary amine and suppresses the formation of the unsaturated hydrocarbon.

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• Original Russian pagination. See C. B. translation.

# PROPERTIES OF BINARY MIXTURES OF ORGANIC COMPOUNDS AS A

## FUNCTION OF ASSOCIATION AND CONCENTRATION

### A. E. Lutskii, E. M. Obukhova, and I. A. Sidorov

The dependence of various physical properties of mixtures on the concentration and especially the extent of their deviation from additivity are extensively used to study intermolecular reaction and association of molecules in solution, either between themselves or with the molecules of the solvent [1]. Here it is postulated that a negative deviation of the viscosity and density of a mixture from additivity [2] or deviation from a linear change in the molar polarization of a dissolved substance, calculated from the dielectric permeability, is a sign that the molecules of the components show association [1]. On this basis it is frequently postulated that the molecules of many substances (chlorobenzene, benzonitrile, etc.), for which other criteria and properties suggest a normal behavior [4], are capable of association [3]. In order to ascertain more accurately the effect of molecular association of the components on the character of the concentration dependence of various physical properties of binary mixtures, we measured the values of one of the equilibrium (density $d_{1,2}$), kinetic (viscosity $\eta_{1,2}$) and electrical (dielectric permeability $\epsilon_{1,2}$) properties of sundry binary mixtures, composed of a constant component 1 (benzene), while as component 2 we took various compounds whose molecules differed mainly only in the dipole moment (isoperiodic compounds), mass (isologs), or in all the properties except shape (monosubstituted benzenes). The methods used to make the measurements and to purify the compounds are given in the dissertation by one of the authors [5]; the measurement results obtained for 25 mixtures of the indicated type are given in Tables 1-10, and for some concentrations and temperatures were presented earlier [6]. The dissertation [5] also has a number of curves, constructed from the data obtained for the relationship between the concentration $N_2$ (in mole fractions) and the described properties, and also the calculated deviations of the latter from additivity using the equation

$$\Delta y = y_{1,2} - [N_2 y_2 + (1 - N_2) y_1]$$

where

$$y = d, \eta, v \text{ or } \epsilon.$$

From the obtained data it follows that contraction of the system occurs when benzene is mixed with its monohalo derivatives, which is confirmed by the measurement results obtained by other authors [3, 7]. The same is also true for mixtures of benzene with bromo- and iodobutane. Only for the mixture benzene-chlorobutane is the $d_{1,2}$-$N_2$ curve somewhat convex to the $N_2$ axis. The $\Delta v_{1,2}$-$N_2$ curves ($\Delta v_{1,2}$ is the deviation of the specific volume of the mixture from additivity) pass through a minimum, in which connection the maximum relative decrease in the volume on mixing increases with the mass of the halogen.

In the case of mixtures of benzene with aromatic isoperiodic compounds a contraction of the system is observed for both normal (except the mixture benzene-ethylbenzene) and associated mixtures, while, on the other hand, an expansion of the system is observed for mixtures of benzene with aliphatic isoperiodic compounds (except the mixture containing ethyl methyl ketone). A similar type of difference in the behavior of the discussed mixtures also follows from the literature data for $d_{1,2}$ [3, 8].

The mixtures with associated components also do not differ from the mixtures with normal (nondissociated) compounds in respect to the character of the change in $\Delta v_{1,2}$ with $N_2$ and $d_{1,2}$ with the temperature. The $\Delta v_{1,2}$-$N_2$

## TABLE 1

Dielectric Permeability $\epsilon_{1,2}$ of Binary Mixtures Composed of Benzene (1) and Halogenated Derivatives (2)

| Component 2 | $N_2$ | $\epsilon^{25}$ | $\epsilon^{50}$ | $\Delta\epsilon \cdot 10^2$ at 25° | Component 2 | $N_2$ | $\epsilon^{25}$ | $\epsilon^{50}$ | $\Delta\epsilon \cdot 10^2$ at 25° |
|---|---|---|---|---|---|---|---|---|---|
| $C_6H_5Cl$ | 0.040 | 2.41 | — | +1 | $n\text{-}C_4H_9\,Cl$ | 0.048 | 2.54 | — | +3 |
| | 0.080 | 2.60 | — | +6 | | 0.098 | 2.80 | — | +4 |
| | 0.121 | 2.76 | — | +9 | | 0.153 | 3.06 | — | +3 |
| | 0.162 | 2.89 | — | +9 | | 0.2 | 3.35 | 3.12 | +8 |
| | 0.2 | 3.00 | 2.87 | +6 | | 0.5 | 4.76 | 4.42 | —2 |
| | 0.5 | 4.02 | 3.81 | +8 | | 0.8 | 6.22 | 5.71 | —7 |
| | 0.8 | 4.95 | 4.64 | +1 | | 1.0 | 7.29 | 6.54 | — |
| | 1.0 | 5.61 | 5.23 | — | | 0.0 | 2.27 | 2.24 | — |
| $C_6H_5Br$ | 0.028 | 2.38 | — | +2 | $n\text{-}C_4H_9Br$ | 0.033 | 2.48 | — | +6 |
| | 0.057 | 2.52 | — | +7 | | 0.66 | 2.66 | — | +8 |
| | 0.086 | 2.60 | — | +6 | | 0.100 | 2.86 | — | +12 |
| | 0.116 | 2.72 | — | +9 | | 0.134 | 3.04 | — | +14 |
| | 0.2 | 3.01 | 2.88 | +11 | | 0.2 | 3.32 | 3.16 | +11 |
| | 0.5 | 3.97 | 3.77 | +13 | | 0.5 | 4.77 | 4.42 | +10 |
| | 0.8 | 4.86 | 4.57 | +9 | | 0.8 | 6.09 | 5.59 | +7 |
| | 1.0 | 5.40 | 5.08 | — | | 1.0 | 6.96 | 6.34 | — |
| $C_6H_5I$ | 0.022 | 2.34 | — | +2 | | | | | |
| | 0.044 | 2.40 | — | +3 | | | | | |
| | 0.066 | 2.50 | — | +7 | | | | | |
| | 0.089 | 2.56 | — | +8 | | | | | |
| | 0.2 | 2.88 | 2.77 | +13 | | | | | |
| | 0.5 | 3.67 | 3.54 | +19 | | | | | |
| | 0.8 | 4.37 | 4.17 | +16 | | | | | |
| | 1.0 | 4.69 | 4.49 | — | | | | | |

curves for many of the studied mixtures, especially the mixtures of benzene with isoperiodic compounds (including associated mixtures), within the limits of experimental error, obey the Biron rule [7, 9]:   $\Delta v_{1,2} = KN_2 (1 - N_2)$ (K is constant at a given temperature).  The density of all of the studied mixtures decreases linearly with increase in the temperature in the studied temperature interval, while the value $\Delta v_{1,2}$, in the case of a negative sign, increases with increase in the temperature, and, to the contrary, decreases if the sign is positive.  Only for mixtures with associated compounds and with a positive sign for $\Delta v_{1,2}$ does the value of the latter increase with the temperature.

All of the investigated mixtures failed to show a linear change of $\epsilon_{1,2}$ with $N_2$.  In harmony with the results of other measurements [3, 10], even the mixtures benzene-chlorobenzene, benzene-ethylbenzene and benzene-diethyl ether, considered to be either ideal or nearly ideal [11], show a noticeable and uniform change in $\Delta\epsilon_{1,2}$ with $N_2$.  In this connection, at the same concentrations $N_2$ and temperatures, those mixtures whose members belong to the same series of halo derivatives show a consistent change in $\Delta\epsilon_{1,2}$ with increase in the mass of the halogen.

Mixtures of benzene with the studied aromatic compounds, except benzyl alcohol, o-cresol and aniline, give a positive $\Delta\epsilon_{1,2}$.  Mixtures of benzene with the studied aliphatic isoperiodic compounds give $\Delta\epsilon_{1,2}$-$N_2$ curves that are always convex to the $N_2$ axis (negative $\Delta\epsilon_{1,2}$).  Here only a larger $|\Delta\epsilon_{1,2}|$ is characteristic for mixtures of benzene with compounds tending to form complexes due to hydrogen bonding between the molecules (propionic acid, butanol).  Evidently, the fact that a mixture has a negative deviation of $\epsilon_{1,2}$ from additivity is not a good criterion that the molecules of the components in the mixture show association.  This is due to the fact that differences in the other properties of the component molecules, such as the dipole moment, polarizability and shape [4, 6], also exert an influence on the sign and value of $\Delta\epsilon_{1,2}$.  It should also be mentioned that but for a few exceptions the sign of $\Delta\epsilon_{1,2}$ coincides with that for $\Delta d_{1,2}$.  Apparently, $\Delta\epsilon_{1,2}$ is associated with the number of component molecules per unit volume of mixture that deviate from additivity.

Within the limits of measurement error, the $\Delta\epsilon_{1,2}$-$N_2$ curves for nearly all of the studied mixtures (including the mixtures with associated components) are quite symmetrical, and the value $\Delta\epsilon_{1,2}$ is satisfactorily calculated using the equation: $\Delta\epsilon_{1,2} = K'N_2 (1 - N_2)$ (K' is a constant).  The mixtures with associated components (alcohols,

TABLE 2

Dielectric Permeability $\epsilon_{1,2}$ of Binary Mixtures Composed of Benzene (1) and Members of Aromatic Isoperiodic Series (2)

| Component 2 | $N_2$ | $\epsilon^{25}$ | $\epsilon^{35}$ | $\epsilon^{45}$ | $\epsilon^{55}$ | $\Delta\epsilon \cdot 10^3$ at 25° |
|---|---|---|---|---|---|---|
| $C_6H_5C_2H_5$ | 0.1 | 2.28 | 2.25 | 2.22 | 2.20 | 0 |
| | 0.2 | 2.30 | 2.28 | 2.26 | 2.24 | 0 |
| | 0.4 | 2.31 | 2.29 | 2.27 | 2.25 | −1 |
| | 0.5 | 2.33 | 2.30 | 2.28 | 2.26 | −1 |
| | 0.6 | 2.34 | 2.32 | 2.30 | 2.29 | −1 |
| | 0 8 | 2.36 | 2.34 | 2.38 | 2.30 | −2 |
| | 1.0 | 2.41 | — | — | — | — |
| $C_6H_5OCH_3$ | 0.1 | 2.49 | 2.46 | 2.42 | 2.38 | +1 |
| | 0.2 | 2.72 | 2.67 | 2.64 | 2.60 | +3 |
| | 0.4 | 3.16 | 3.10 | 3.06 | 3.01 | +6 |
| | 0.5 | 3.40 | 3.32 | 3.27 | 3.22 | +9 |
| | 0.6 | 3.63 | 3.54 | 3.48 | 3.42 | +11 |
| | 0.8 | 4.01 | 3.93 | 3.83 | 3.77 | +8 |
| | 1.0 | 4.35 | — | — | — | — |
| $C_6H_5CH_2OH$ | 0.1 | 2.77 | 2.74 | 2.70 | 2.66 | — |
| | 0.2 | 3.40 | 3.34 | 3.27 | 3.22 | — |
| | 0.5 | 6.25 | 5.94 | 5.68 | 5.42 | — |
| $C_6H_4(CH_3)OH\text{-}o$ | 0.1 | 2.64 | 2.60 | 2.55 | 2.51 | −10 |
| | 0.2 | 3.04 | 2.99 | 2.93 | 2.88 | −17 |
| | 0.4 | 3.91 | 3.31 | 3.71 | 3.60 | −24 |
| | 0.5 | 4.36 | 4.25 | 4.12 | 4.00 | −28 |
| | 0.6 | 4.87 | 4.70 | 7.54 | 4.41 | −22 |
| | 0.8 | 5.96 | 5.72 | 5.50 | 5.25 | −7 |
| | 1.0 | 6.97 | — | — | — | — |
| $C_6H_5CN$ | 0.2 | 6.98 | 6.72 | 6.50 | 6.34 | — |

TABLE 3

Dielectric Permeability $\epsilon_{1,2}$ of Binary Mixtures Composed of Benzene (1) and Members of Aliphatic Isoperiodic Series (2)

| Component 2 | $N_2$ | $\epsilon^{20}$ | $\epsilon^{30}$ | $\epsilon^{40}$ | $\epsilon^{0}$ | $\Delta\epsilon \cdot 10^3$ at 25° |
|---|---|---|---|---|---|---|
| $(C_2H_5)_2NH$ | 0.2 | 2.58 | 2.51 | — | — | −3 |
| | 0.4 | 2.88 | 2.81 | — | — | −7 |
| | 0.5 | 3.04 | 2.95 | — | — | −8 |
| | 0.6 | 3.22 | 3.10 | — | — | −7 |
| | 0.8 | 3.56 | 3.41 | — | — | −6 |
| | 1.0 | 3.96 | — | — | — | — |
| $(C_2H_5)_2O$ | 0.2 | 2.66 | — | — | — | −4 |
| | 0.4 | 3.06 | — | — | — | −4 |
| | 0.5 | 3.28 | — | — | — | −4 |
| | 0.6 | 3.48 | — | — | — | −5 |
| | 0.8 | 3.91 | — | — | — | −4 |
| | 1.0 | 4.265 (25°) | — | — | — | — |
| $CH_3COOCH_3$ | 0.5 | 4.82 | 4.66 | — | — | — |
| | 1.0 | 7.3 | — | — | — | — |

TABLE 3 (continued)

| Component 2 | $N_2$ | $\epsilon^{20}$ | $\epsilon^{30}$ | $\epsilon^{40}$ | $\epsilon^{50}$ | $\Delta\epsilon \cdot 10^2$ at 25° |
|---|---|---|---|---|---|---|
| HCOOC$_2$H$_5$ | 0.2 | 3.33 | 3.26 | — | — | —17 |
| | 0.4 | 4.49 | 4.36 | — | — | — |
| | 0.5 | 5.11 | 4.97 | — | — | — |
| | 1.0 | 8.4 | — | — | — | — |
| C$_2$H$_5$COOH | 0.2 | 2.36 | 2.34 | 2.32 | 2.30 | —10 |
| | 0.4 | 2.49 | 2.48 | 2.47 | 2.46 | —15 |
| | 0.5 | 2.66 | 2.56 | 2.55 | 2.55 | —17 |
| | 0.8 | 2.92 | 2.93 | 2.96 | 2.96 | —8 |
| | 1.0 | 3.19 | — | — | — | — |
| n-C$_4$H$_9$OH | 0.2 | 3.46 | 3.35 | 3.25 | 3.19 | $\sim$ —192 |
| | 0.4 | 8.03 | 7.40 | 6.71 | 6.08 | — |
| | 1.0 | 17.8 [13] | | | | |
| CH$_3$COC$_2$H$_5$ | 0.2 | 4.64 | 4.49 | 4.37 | 4.24 | $\sim$ —78 |
| | 1.0 | 18.0 [13] | | | | |

TABLE 4

Dielectric Permeability $\epsilon_{1,2}$ and Deviations from Additivity $\Delta\epsilon_{1,2}$ of Mixtures of Benzene (1) with Its Derivatives (2)

| Component 2 | $N_2$ | $\epsilon^{25}$ | $\epsilon^{65}$ | $\Delta\epsilon^{25}$ |
|---|---|---|---|---|
| C$_6$H$_5$OC$_2$H$_5$ | 0.2 | 2.81 | 2.69 | —0.13 |
| | 0.5 | 3.48 | 3.30 | +0.18 |
| | 1.0 | 4.35 | 4.07 | — |
| C$_6$H$_5$N(CH$_3$)$_2$ | 0.2 | 3.03 | 2.88 | +0.21 |
| | 0.5 | 3.94 | 3.71 | +0.28 |
| | 1.0 | 5.05 | 4.70 | — |
| C$_6$H$_5$NH$_2$ | 0.2 | 3.09 | 2.94 | —0.13 |
| | 0.5 | 4.44 | 4.12 | —0.22 |
| | 1.0 | 7.07 | 6.34 | — |
| C$_6$H$_5$CH$_2$Cl | 0.2 | 3.31 | 3.16 | +0.15 |
| | 0.5 | 4.72 | 4.48 | +0.17 |
| | 1.0 | 6.85 | 6.34 | — |
| C$_6$H$_5$COOC$_2$H$_5$ | 0.2 | 3.32 | 3.13 | +0.30 |
| | 0.5 | 4.56 | 4.25 | +0.40 |
| | 1.0 | 6.06 | 5.56 | — |
| C$_6$H$_5$CHO | 0.1 | 3.62 | 3.40 | $\sim$ —0.22 |
| | 0.2 | 5.02 | 4.64 | $\sim$ —0.49 |
| | 1.0 | 18.0 [13] | | |
| C$_6$H$_5$NO$_2$ | 0.2 | — | 6.50 | — |
| C$_6$H$_5$OH | 0.2 | 3.40 | 3.11 | — |
| | 0.5 | 6.10 | 5.14 | — |

# TABLE 5

Density of Mixtures of $C_6H_6$ (1) and Halo Derivatives at Various Temperatures

| Component 2 | $N_2$ | $d^{25}$ | $d^{35}$ | $d^{45}$ | $d^{50}$ | $\Delta v \cdot 10^4$ | |
|---|---|---|---|---|---|---|---|
| | | | | | | 25° | 50° |
| n-$C_4H_9Cl$ | 0.000 | 0.8734 | 0.8628 | 0.8721 | 0.8468 | — | — |
| | 0.098 | 0.8756 | 0.8629 | 0.8522 | 0.8466 | +4 | +4 |
| | 0.153 | 0.8737 | 0.8630 | 0.8523 | 0.8468 | 1 | 5 |
| | 0.800 | 0.8773 | — | — | 0.8793 | 6 | 0 |
| | 1.000 | 0.8787 | 0.8675 | 0.8561 | 0.8504 | — | — |
| n-$C_4H_9Br$ | 0.066 | 0.9038 | 0.8929 | 0.8821 | 0.8767 | −58 | −65 |
| | 0.100 | 0.9191 | 0.9080 | 0.8970 | 0.8915 | −80 | −86 |
| | 0.134 | 0.9344 | 0.9232 | 0.9120 | 0.9064 | −101 | −107 |
| | 0.800 | 1.1972 | — | — | 1.1623 | −73 | −77 |
| | 1.000 | 1.2638 | 1.2493 | 1.2348 | 1.2275 | — | — |
| n-$C_4H_9I$ | 0.075 | 0.9404 | 0.9292 | 0.9179 | 0.9123 | −143 | −150 |
| | 0.100 | 0.9629 | 0.9575 | 0.9411 | 0.9344 | −186 | −195 |
| | 0.800 | 1.4784 | — | — | 1.4387 | −118 | −120 |
| | 1.000 | 1.5989 | 1.5823 | 1.5658 | 1.5575 | — | — |
| $C_6H_5Cl$ | 0.080 | 0.8941 | 0.8833 | 0.8724 | 0.8669 | −31 | −27 |
| | 0.121 | 0.9044 | 0.8936 | 0.8828 | 0.8775 | −45 | −46 |
| | 0.162 | 0.9147 | 0.9039 | 0.8932 | 0.8879 | −53 | −55 |
| | 0.800 | 1.0602 | — | — | 1.0329 | −42 | −42 |
| | 1.000 | 1.1010 | 1.0902 | 1.0793 | 1.0739 | — | — |
| $C_6H_5Br$ | 0.0867 | 0.9355 | 0.9244 | 0.9133 | 0.9078 | −102 | −102 |
| | 0.116 | 0.9565 | 0.9452 | 0.9340 | 0.9283 | −130 | −129 |
| | 0.800 | 1.3811 | — | — | 1.3483 | −83 | −86 |
| | 1.000 | 1.4885 | 1.4752 | 1.4616 | 1.4543 | — | — |
| $C_6H_5I$ | 0.0668 | 0.9512 | 0.9401 | 0.9291 | 0.9235 | −166 | −173 |
| | 0.0896 | 0.9774 | 0.9661 | 0.9549 | 0.9492 | −208 | −215 |
| | 0.800 | 1.6596 | — | — | 1.6235 | −118 | −121 |
| | 1.000 | 1.8163 | 1.8013 | 1.7862 | 1.7782 | — | — |

# TABLE 6

Density of Mixtures of $C_6H_6$ (1) and Members of the Same Aromatic Isoperiodic Series (2) at Various Temperatures

| Component 2 | $N_2$ | $d^{25}$ | $d^{35}$ | $d^{45}$ | $d^{50}$ | $\Delta v \cdot 10^4$ | |
|---|---|---|---|---|---|---|---|
| | | | | | | 25° | 50° |
| $C_6H_5C_2H_5$ | 0.1 | 0.8715 | 0.8610 | 0.8506 | 0.8454 | +10 | +8 |
| | 0.2 | 0.8698 | 0.8595 | 0.8494 | 0.8443 | +18 | +15 |
| | 0.4 | 0.8672 | 0.8574 | 0.8475 | 0.8427 | +24 | +20 |
| | 0.5 | 0.8660 | 0.8565 | 0.8470 | 0.8422 | +24 | +17 |
| | 0.6 | 0.8650 | 0.8557 | 0.8464 | 0.8417 | +24 | +17 |
| | 0.8 | 0.8635 | 0.8545 | 0.8454 | 0.8410 | +15 | +9 |
| | 1.0 | 0.8624 | 0.8536 | 0.8448 | 0.8404 | — | — |
| $C_6H_5OCH_3$ | 0.1 | 0.8874 | 0.8768 | 0.8662 | 0.8610 | −31 | −34 |
| | 0.2 | 0.9007 | 0.8904 | 0.8801 | 0.8750 | −51 | −60 |
| | 0.4 | 0.9256 | 0.9156 | 0.9056 | 0.9007 | −69 | −81 |
| | 0.5 | 0.9373 | 0.9273 | 0.9175 | 0.9126 | −69 | −79 |
| | 0.6 | 0.9485 | 0.9386 | 0.9289 | 0.9240 | −63 | −71 |
| | 0.8 | 0.9696 | 0.9600 | 0.9504 | 0.9456 | −39 | −43 |
| | 1.0 | 0.9891 | 0.9797 | 0.9703 | 0.9656 | — | — |

| Component 2 | $N_2$ | $d^\circ$ | $d''$ | $d^{45}$ | $d''$ | $\Delta c \cdot 10'$ | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| | | | | | | 25° | 50° |
| C$_6$H$_5$CH$_2$OH | 0.1 | 0.8932 | 0.8827 | 0.8722 | 0.8670 | −40 | −40 |
| | 0.2 | 0.9122 | 0.9021 | 0.8920 | 0.8870 | −67 | −7? |
| | 0.5 | 0.9651 | 0.9561 | 0.9470 | 0.9426 | −91 | −100 |
| | 0.8 | 1.0122 | 1.0039 | 0.9957 | 0.9915 | −53 | −60 |
| | 1.0 | 1.0401 | 1.0322 | 1.0244 | 1.0206 | — | — |
| C$_6$H$_5$CHO | 0.1 | 0.8926 | 0.8822 | 0.8718 | 0.8665 | −35 | −45 |
| | 0.2 | 0.9115 | 0.9012 | 0.8912 | 0.8861 | −59 | −71 |
| | 0.4 | 0.9472 | 0.9374 | 0.9278 | 0.8230 | −77 | −92 |
| | 0.5 | 0.9642 | 0.9548 | 0.9454 | 0.9407 | −77 | −93 |
| | 0.6 | 0.9806 | 0.9713 | 0.9621 | 0.9575 | −72 | −87 |
| | 0.8 | 1.0119 | 1.0029 | 0.9940 | 0.9896 | −41 | −52 |
| | 1.0 | 1.0421 | 1.0332 | 1.0243 | 1.0199 | — | — |
| C$_6$H$_5$CN | 1.0 | 1.0408 | 1.0321 | 1.0233 | 1.0189 | | |
| | 0.2 | 0.9031 | 0.8930 | 0.8830 | 0.8780 | −53 | −66 |

## TABLE 7

Density of Mixtures of C$_6$H$_6$ (I) and Members of the Same Aliphatic Isoperiodic Series (2) at Various Temperatures

| Component 2 | $N_2$ | $d^{20}$ | $d^{30}$ | $d^{35}$ | $d^{45}$ | $\Delta v \cdot 10^4$ | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| | | | | | | 20° | 35° |
| (C$_2$H$_5$)$_2$NH | 0.2 | 0.8391 | 0.8285 | 0.8232 | — | +70 | +68 |
| | 0.4 | 0.8022 | 0.7917 | 0.7865 | — | +110 | +104 |
| | 0.5 | 0.7847 | 0.7743 | 0.7691 | — | +117 | +109 |
| | 0.6 | 0.7686 | 0.7582 | 0.7529 | — | +100 | +91 |
| | 0.8 | 0.7356 | 0.7250 | 0.7197 | — | +78 | +70 |
| | 1.0 | 0.7051 | 0.6943 | 0.6885 | — | — | — |
| (C$_2$H$_5$)$_2$O | 0.2 | 0.8440 | — | — | — | +25 | — |
| | 0.4 | 0.8105 | — | — | — | +33 | — |
| | 0.5 | 0.7941 | — | — | — | +35 | — |
| | 0.6 | 0.7778 | — | — | — | +33 | — |
| | 0.8 | 0.7457 | — | — | — | +20 | — |
| | 1.0 | 0.7138 | — | — | — | — | — |
| C$_2$H$_5$COOH | 0.2 | 0.8961 | 0.8854 | 0.8800 | 0.8699 | +69 | +71 |
| | 0.4 | 0.9159 | 0.9051 | 0.8997 | 0.8889 | +103 | +106 |
| | 0.5 | 0.9269 | 0.9160 | 0.9106 | 0.8998 | +106 | +110 |
| | 0.8 | 0.9640 | 0.9531 | 0.9477 | 0.9368 | +69 | +71 |
| | 1.0 | 0.9934 | 0.9824 | 0.9770 | 0.9661 | — | — |
| n-C$_4$H$_9$OH | 0.2 | 0.8630 | 0.8526 | 0.8474 | 0.8370 | +25 | +32 |
| | 0.4 | 0.8489 | 0.8390 | 0.8341 | 0.8243 | +30 | +37 |
| | 0.5 | 0.8421 | 0.8326 | 0.8279 | 0.8184 | +29 | +34 |
| | 0.6 | 0.8356 | 0.8264 | 0.8210 | 0.8126 | +23 | +28 |
| | 0.8 | 0.8226 | 0.8141 | 0.8098 | 0.8014 | +10 | +14 |
| | 1.0 | 0.8095 | 0.8047 | 0.7978 | 0.7900 | — | — |
| CH$_3$COOCH$_3$ | 0.5 | 0.9004 | 0.8887 | 0.8829 | — | +64 | +59 |
| | 1.0 | 0.9325 | 0.9191 | 0.9124 | — | — | — |
| HCOOC$_2$H$_5$ | 0.2 | 0.8832 | 0.8721 | 0.8665 | — | +29 | +29 |
| | 0.4 | 0.8889 | 0.8774 | 0.8716 | — | +43 | +42 |
| | 0.5 | 0.8920 | 0.8804 | 0.8745 | — | +46 | +43 |
| | 0.8 | 0.9036 | 0.8910 | 0.8849 | — | +26 | +29 |
| | 1.0 | 0.9125 | 0.8955 | 0.8931 | — | — | — |
| CH$_3$COC$_2$H$_5$ | 0.2 | 0.8646 | 0.8538 | 0.8485 | 0.8378 | −6 | −7 |
| | 0.4 | 0.8502 | 0.8395 | 0.8343 | 0.8237 | −10 | −13 |
| | 0.5 | 0.8430 | 0.8324 | 0.8271 | 0.8166 | −12 | −15 |
| | 0.6 | 0.8357 | 0.8251 | 0.8198 | 0.8092 | −13 | −15 |
| | 0.8 | 0.8201 | 0.8094 | 0.8041 | 0.7935 | 0 | 0 |
| | 1.0 | 0.8055 | 0.7948 | 0.7895 | 0.7789 | — | — |

## TABLE 8

Viscosity $\eta_{1,2} \cdot 10^5$ of Mixtures of Benzene and Halo Derivatives (Isologs) at Various Temperatures

| Halo derivative (2) | $N_2$ | $\eta^{25}$ | $\eta^{35}$ | $\eta^{45}$ | $\eta^{50}$ | $\Delta\eta \cdot 10^3$ | |
|---|---|---|---|---|---|---|---|
| | | | | | | 25° | 50° |
| n-C$_4$H$_9$Cl | 0.000 | 602 | 527 | 464 | 436 | — | — |
| | 0.098 | 557 | 492 | 437 | 417 | −0.28 | −0.09 |
| | 0.153 | 542 | 481 | 428 | 404 | −0.33 | −0.17 |
| | 0.800 | 454 | — | — | 358 | −0.25 | −0.12 |
| | 1.000 | 428 | 390 | 356 | 340 | — | — |
| n-C$_4$H$_9$Br | 0.066 | 588 | 518 | 459 | 432 | −0.14 | −0.06 |
| | 0.100 | 583 | 515 | 457 | 431 | −0.19 | −0.09 |
| | 0.134 | 574 | 510 | 454 | 428 | −0.16 | −0.10 |
| | 1.000 | 606 | 552 | 502 | 476 | — | — |
| C$_6$H$_5$Cl | 0.080 | 613 | 537 | 475 | 444 | −0.02 | −0.01 |
| | 0.121 | 620 | 544 | 482 | 451 | 0.0 | −0.01 |
| | 0.162 | 623 | 547 | 486 | 454 | −0.03 | −0.02 |
| | 0.800 | 718 | — | — | 541 | −0.06 | −0.02 |
| | 1.000 | 750 | 669 | 601 | 566 | — | — |
| C$_6$H$_5$Br | 0.0867 | 636 | 558 | 492 | 461 | −0.05 | −0.05 |
| | 0.116 | 649 | 568 | 504 | 470 | −0.07 | −0.07 |
| | 0.800 | 960 | — | — | 711 | −0.07 | −0.02 |
| | 1.000 | 1056 | 934 | 836 | 784 | — | — |
| C$_6$H$_5$I | 0.0668 | 646 | 565 | 499 | 469 | −0.16 | −0.10 |
| | 0.0896 | 660 | 578 | 512 | 478 | −0.22 | −0.15 |
| | 0.800 | 1274 | — | — | 917 | −0.33 | −0.16 |
| | 1.000 | 1513 | 1318 | 1162 | 1083 | — | — |

## TABLE 9

Viscosity $\eta_{1,2} \cdot 10^5$ of Mixtures of Benzene (1) and Members of Aromatic Series of Isoperiodic Compounds (2) at Various Temperatures

| Component 2 | $N_2$ | $\eta^{25}$ | $\eta^{35}$ | $\eta^{45}$ | $\eta^{50}$ | $\Delta\eta \cdot 10^5$ | |
|---|---|---|---|---|---|---|---|
| | | | | | | 25° | 50° |
| C$_6$H$_5$C$_2$H$_5$ | 0.1 | 599 | 528 | 468 | 440 | −5 | 0 |
| | 0.2 | 601 | 530 | 471 | 443 | −6 | −1 |
| | 0.4 | 603 | 535 | 477 | 449 | −8 | −2 |
| | 0.5 | 607 | 538 | 481 | 453 | −7 | −2 |
| | 0.6 | 608 | 542 | 484 | 456 | −8 | −3 |
| | 0.8 | 616 | 551 | 492 | 466 | −4 | 0 |
| | 1.0 | 625 | 560 | 502 | 474 | — | — |
| C$_6$H$_5$OCH$_3$ | 0.1 | 635 | 556 | 489 | 460 | −5 | −1 |
| | 0.2 | 671 | 587 | 517 | 485 | −8 | −2 |
| | 0.4 | 742 | 649 | 570 | 533 | −14 | −4 |
| | 0.5 | 782 | 680 | 597 | 559 | −12 | −4 |
| | 0.6 | 821 | 715 | 626 | 585 | −11 | −3 |
| | 0.8 | 907 | 785 | 684 | 640 | −2 | +1 |
| | 1.0 | 986 | 851 | 739 | 690 | — | — |
| o-C$_6$H$_4$(CH$_3$)OH | 0.1 | 704 | 609 | 531 | 497 | −587 | −178 |
| | 0.2 | 849 | 727 | 623 | 578 | −1131 | −337 |
| | 0.4 | 1319 | 1073 | 894 | 815 | −2039 | −572 |
| | 0.5 | 1661 | 1334 | 1084 | 981 | −2386 | −652 |
| | 0.6 | 2148 | 1668 | 1331 | 1186 | −2589 | −586 |
| | 0.8 | 3874 | 2766 | 2067 | 1807 | −2241 | −544 |
| | 1.0 | 7493 | 4853 | 3359 | 2830 | — | — |

TABLE 9 (continued)

| Component 2 | $N_2$ | $\eta^{25}$ | $\eta^{35}$ | $\eta^{43}$ | $\eta^{50}$ | $\Delta\eta \cdot 10^5$ | |
|---|---|---|---|---|---|---|---|
| | | | | | | 25° | 50° |
| $C_6H_5CH_2OH$ | 0.1 | 700 | 597 | 526 | 493 | −369 | −158 |
| | 0.2 | 855 | 714 | 617 | 575 | −682 | −292 |
| | 0.5 | 1712 | 1379 | 1139 | 1026 | −1227 | −487 |
| | 0.8 | 3267 | 2433 | 1904 | 1695 | −1074 | −467 |
| | 1.0 | 5276 | 3891 | 2945 | 2591 | — | — |
| $C_6H_5CHO$ | 0.1 | 655 | 583 | 509 | 477 | −28 | −13 |
| | 0.2 | 714 | 625 | 551 | 517 | −50 | −27 |
| | 0.4 | 847 | 742 | 667 | — | −79 | — |
| | 0.5 | 928 | 809 | 711 | 665 | −78 | −42 |
| | 0.6 | 1012 | 885 | 773 | 724 | −56 | −22 |
| | 1.0 | 1411 | 1215 | 1051 | 975 | — | — |
| $C_6H_5CN$ | 0.2 | 688 | 605 | 532 | 498 | −43 | −24 |
| | 1.0 | 1249 | 1071 | 931 | 866 | — | — |

## TABLE 10

Viscosity $\eta_{1,2} \cdot 10^5$ of Mixtures of Benzene (I) and Members of Aliphatic Series of Isoperiodic Compounds (2) at Various Temperatures

| Component 2 | $N_2$ | $\eta^{20}$ | $\eta^{30}$ | $\eta^{35}$ | $\eta^{45}$ | $\Delta\eta \cdot 10^5$ | |
|---|---|---|---|---|---|---|---|
| | | | | | | 20° | 35° |
| $(C_2H_5)_2NH$ | 0.2 | 522 | 463 | 438 | — | −60 | −38 |
| | 0.4 | 440 | 393 | 374 | — | −76 | −52 |
| | 0.5 | 411 | 367 | 350 | — | −73 | −51 |
| | 0.6 | 387 | 348 | 333 | — | −64 | −42 |
| | 0.8 | 349 | 314 | 298 | — | −36 | −27 |
| | 1.0 | 320 | 288 | 274 | — | — | — |
| $(C_2H_5)_2O$ | 0.2 | 504 | — | — | — | −14 | — |
| | 0.4 | 407 | — | — | — | −81 | — |
| | 0.5 | 371 | — | — | — | −77 | — |
| | 0.6 | 339 | — | — | — | −70 | — |
| | 0.8 | 289 | — | — | — | −40 | — |
| | 1.0 | 250 | — | — | — | — | — |
| $C_2H_5COOH$ | 0.2 | 660 | 575 | 542 | 480 | −78 | −58 |
| | 0.4 | 700 | 610 | 575 | 510 | −129 | −99 |
| | 0.5 | 734 | 639 | 602 | 533 | −140 | −108 |
| | 0.8 | 889 | 774 | 729 | 643 | −121 | −92 |
| | 1.0 | 1101 | 944 | 894 | 783 | — | — |
| $n\text{-}C_4H_9OH$ | 0.2 | 714 | 604 | 562 | 490 | −387 | −254 |
| | 0.4 | 898 | 746 | 687 | 584 | −657 | −419 |
| | 0.5 | 1054 | 864 | 791 | 662 | −727 | −459 |
| | 0.6 | 1279 | 1021 | 924 | 761 | −729 | −471 |
| | 0.8 | 1920 | 1490 | 1335 | 1062 | −542 | −350 |
| | 1.0 | 2916 | 2253 | 1974 | 1539 | — | — |
| $CH_3COOCH_3$ | 0.5 | 480 | 428 | 406 | — | — | −34 |
| | 1.0 | 411 | 372 | 354 | — | — | — |
| $HCOOC_2H_5$ | 0.2 | 558 | 491 | 465 | — | −43 | −29 |
| | 0.4 | 501 | 446 | 427 | — | −54 | −34 |
| | 0.5 | 482 | 430 | 409 | — | −50 | −35 |
| | 0.8 | 435 | 391 | 373 | — | −29 | −21 |
| | 1.0 | 418 | 378 | 361 | — | — | — |
| $CH_3COC_2H_5$ | 0.2 | 569 | 498 | 471 | 421 | −31 | −21 |
| | 0.4 | 511 | 454 | 431 | 388 | −41 | −27 |
| | 0.5 | 487 | 434 | 414 | 373 | −42 | −27 |
| | 0.6 | 471 | 420 | 401 | 362 | −34 | −22 |
| | 0.8 | 435 | 391 | 373 | 339 | −23 | −16 |
| | 1.0 | 411 | 370 | 355 | 322 | — | — |

acids, amines) show only much higher values of the constant K'. In the temperature range studied all of the mixtures show a decrease in $\epsilon_{1,2}$ with increase in the temperature [3, 12]. A characteristic of the mixtures with the indicated associated compounds is either an abnormally low (for the acids) or, to the contrary, a high (for the alcohols and phenols) value of $\Delta\epsilon/\Delta t$.

The data for the viscosities of the studied mixtures also do not show any qualitative difference in the character of the relationship between $\eta_{1,2}$ and $N_2$ for the mixtures with associated and nonassociated components. The $\eta_{1,2}$-$N_2$ curves for all the mixtures, including those with acids, alcohols and phenols as the 2 components, are characterized by a negative deviation of $\eta_{1,2}$ from additivity. Here many highly polar members of the isoperiodic series give mixtures with benzene that are characterized by extremely high absolute values of $\Delta\eta_{1,2}$. Consequently, the characteristic of mixtures with associated compounds is not the sign of $\Delta\eta_{1,2}$, but instead of its abnormally high absolute value. The above-mentioned difference between mixtures of benzene with aromatic and with aliphatic compounds is manifested in the case of viscosity by the fact that for mixtures of benzene with its halogenated derivatives $|\Delta\eta_{1,2}|$ increases in the order I > Br > Cl, and for mixtures of benzene with halogenated derivatives of butane, to the contrary, in the order Cl > Br > I.

Mixtures with associated components show a quantitative, and not a qualitative, difference from mixtures with normal compounds also in respect to the change in $\eta_{1,2}$ and $\Delta\eta_{1,2}$ with the temperature. In the studied temperature interval the $\eta_{1,2}$-t curves for all of the mixtures are convex to the temperature axis, the only difference being that the curves for the mixtures with associated compounds show a sharper deflection. For all of the studied mixtures the value $|\Delta\eta_{1,2}|$ decreases with increase in the temperature, in which connection this decrease is   greater   for both the mixtures with highly polar and associated compounds.

## SUMMARY

1.  The values of the dielectric permeability ($\epsilon_{1,2}$), density ($d_{1,2}$) and viscosity ($\eta_{1,2}$) for binary mixtures of benzene with various aliphatic and aromatic compounds were measured.

2.  The mixtures composed of benzene and associated compounds (alcohols, acids, phenols, aniline) obey the same laws as do mixtures with normal compounds for the change in $d_{1,2}$, $\epsilon_{1,2}$ and $\eta_{1,2}$ with concentration and temperature, and show comparable deviations from additivity. The first mixtures differ from the second not in the laws of change, but only in the abnormal (when compounds of the same type are compared) values of the indicated constants and in their degree of change with concentration and temperature.

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# EFFECT OF DILUTION ON THE ACTIVITY OF COPPER CATALYST IN THE DEHYDROGENATION OF BUTYL ALCOHOL

B. N. Dolgov, V. V. Mazurek, and V. A. Krol'

In a previous communication [1] it was shown by one of us that in the dehydrogenation of butyl alcohol over copper catalyst it is possible to achieve a substantial increase in the yield of aldehyde if the starting alcohol is diluted with pure hydrogen in a mole ratio of $1:1$. Such dilution during dehydrogenation is quite frequently used in industrial heterogeneous catalysis [2-7]. However, the dehydrogenation of alcohols in a stream of hydrogen has not been subjected to a systematic study, and only isolated statements can be found in the literature on the matter (for example, the dehydrogenation of octanol in a stream of hydrogen) [8].
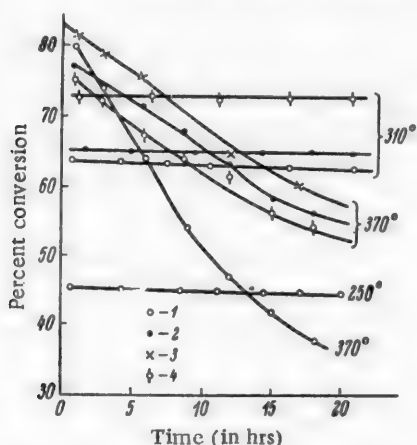


Fig. 1. Change of the percent conversion of butyl alcohol with time as a function of the experiment temperature and the addition of gaseous diluents. 1) Without gas addition, 2) with the addition of nitrogen, 3) with the addition of carbon dioxide; 4) with the addition of hydrogen.

It is assumed that the role played by added gases reduces to protecting the catalyst from poisoning [3, 7], either by suppressing side reactions that could lead to a poisoning of the catalyst surface [7], or by removing difficultly desorbed products, formed during reaction, from the surface [3, 9-11]. One of us had expressed the theory [11] that hydrogen plays the role of a catalyst in the acid-free esterification of alcohols, which takes place over dehydrogenation catalysts, and enters into the intermediate reactions.

In the present study we sought to determine whether the influence exerted by hydrogen in the dehydrogenation of alcohols is due to its specific action or whether it reduces to maintaining a constant catalyst activity; we also sought to determine whether other gases would exert a similar effect and to what a reduction in catalytic activity was due to. With this in mind we ran some experiments on the dehydrogenation of butyl alcohol over copper catalyst in the presence of various gases (hydrogen, nitrogen, carbon dioxide).

It must be remembered that the dehydrogenation of alcohols over copper catalyst is accompanied by acid-free esterification reactions, the result of further transformations of the aldehyde, and also by the formation of small amounts of butyric acid. For this reason we took as the criterion of catalyst activity in the dehydrogenation not the aldehyde yield, but instead the percent of alcohol conversion. Still, to more completely characterize the activity of the catalyst, we also took into consideration its activity in the acid-free esterification reaction, which made it possible to make some additional conclusions relative to the changes in the catalyst surface with time.

The experiments were run at 250, 310 and 370°, with a constant space velocity of 160. The method of operation was the same as that employed earlier [1]. The yields of the main reaction products as a function of the time and dilution with a gas ($H_2$, $N_2$, $CO_2$) are shown in Figs. 1 and 2.
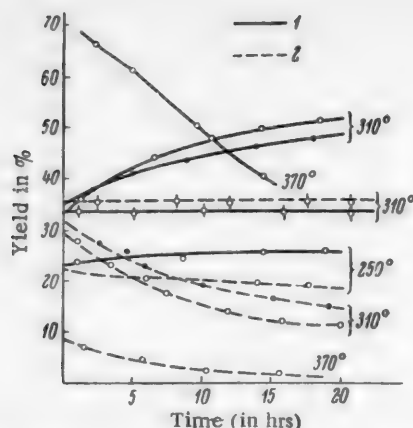
Fig. 2. Relationship between the yield of main reaction products and the time. 1) Aldehyde, 2) ester.

As can be seen from Figs. 1 and 2, at 250° the percent of alcohol conversion and the catalyzate composition fail to show any substantial change in 20 hrs of continuous catalyst operation even without the addition of any gas to the reaction zone.

At 310° in 30 hrs of catalyst operation without the addition of a gas the percent of alcohol conversion remains constant, but the ratio of the reaction products in the catalyzate changes substantially: the yield of aldehyde increases and the yield of ester decreases. The addition of nitrogen in a mole ratio of 1:1 is without effect on the operation of the catalyst. To the contrary, the addition of hydrogen in the same ratio assures a constant operation of the catalyst as regards the yields of aldehyde and ester.

At 370° the percent conversion drops quite sharply even after 9-10 hrs of catalyst operation. The addition of nitrogen, hydrogen or carbon dioxide retards the rate of catalyst deactivation. The nature of the gas is not important here. At the start of experiment (without the addition of a gas) there is a rapid increase in the aldehyde yield, corresponding to a slow increase at 310°, and then the aldehyde yield drops.

The blowing of the deactivated catalyst with hydrogen at 300-350° for 10-12 hrs does not restore its activity. However, the activity of the catalyst is completely restored by passing a slow stream of air over it at 250°, followed by reduction with hydrogen.

TABLE 1

Results of the Combustion of Two Weighed Samples of Catalyst

| Time of catalyst operation (in hrs) | Weight of catalyst (in g) | Amount of substance consumed (in g) | Obtained (in g) | |
|---|---|---|---|---|
| | | | $CO_2$ | $H_2O$ |
| 1 | 7.4 | 0.0066 | 0.0164 | 0.0052 |
| 15 | 6.9 | 0.0334 | 0.0840 | 0.0266 |

To establish the nature of the difficultly desorbed products blocking the catalyst surface, a known amount of the poisoned contact was combusted in a furnace set up for elemental analysis. In this way we were able to establish the presence of unsaturated compounds on the catalyst surface, to which the formula of $(C_4H_6O)_n$ could be assigned. The data on the combustion of two weighed samples of catalyst with a different degree of poisoning are given in Table 1.

Consequently, the following reactions proceed on the catalyst surface: 1) dehydration of alcohol to aldehyde, 2) acid-free esterification, in which the aldehyde participates, and 3) formation of high-molecular unsaturated compound.

The first two reactions represent stages in the acid-free esterification of alcohols, in which the aldehyde is an intermediate product. The reaction for the dehydrogenation of an alcohol to the aldehyde is monomolecular, and one active center is required for it to progress. A doublet is probably the active center here.

The ester condensation reaction is independent of whether it reduces to the condensation of two molecules of aldehyde or of a molecule of aldehyde and alcohol, it is bimolecular in nature, and it proceeds on two adjacent active centers, apparently, on two doublets. The difficultly desorbed compounds that are formed remain on the active centers of the surface and poison the catalyst. However, the process of poisoning the active centers proceeds by a law of chance, and here the number of adjacent pairs of active centers naturally decreases much more rapidly than does the total number of active centers. This is supported by the calculations of Rideal [12], who

showed that to terminate the catalytic hydrogenation of benzene it is sufficient to poison only a part of the active centers. At the same time such a partially poisoned catalyst is still capable of catalyzing the hydrogenation of ethylene. This is associated with the fact that to hydrogenate benzene a sextet, which is composed of three adjacent doublets, is required, while to hydrogenate ethylene requires only one doublet.

In the presented experiments a reduction in catalyst activity is first manifested not in the total percent of alcohol conversion, but in a reduction in the yield of ester. Here an increase in the yield of aldehyde is observed, since the probability of its further transformation drops sharply due to the relatively rapid decrease in the number of adjacent pairs. Later, when a substantial portion of the active centers has become poisoned, both the total percent of conversion and the yield of aldehyde begin to decrease noticeably. At 310° in 30 hrs of catalyst operation we were unable to reach the point of a reduction in the aldehyde yield; however, this reduction was clearly expressed at a higher temperature (370°). Dilution with a gas reduces the partial pressure of all of the reactants and this is most strongly manifested in the case of the higher order reactions, and in particular, in the formation of the high-molecular compound.

That the influence of various gases proves to be extremely close at 370° is probably due to the fact that at high temperatures the adsorption of all of the indicated gases on copper is apparently slight, and all of the adsorption coefficients are close in their absolute values.

The situation is entirely different at lower temperatures (310°). Here the hydrogen plays a peculiar specific role. It apparently takes an active part in the acid-free esterification reaction as a supplemental catalyst, which is in agreement with the data of some earlier investigations made by one of us [11]. In addition, at lower temperatures hydrogen is capable of hydrogenating those unsaturated compounds whose condensation leads to the formation of high-molecular compounds, serving to poison the catalyst surface.

## EXPERIMENTAL

All of the experiments were run in an aluminum block furnace, which made it possible to maintain a quite constant experimental temperature. As catalyst we took pure copper, which was prepared by the precipitation of cupric nitrate with caustic. For each experiment we took a fresh portion of catalyst, which was reduced with

TABLE 2

Results of the Experiments with Butyl Alcohol at 310°

| Time (in hrs) | In presence of nitrogen | | | | In presence of hydrogen | | | |
|---|---|---|---|---|---|---|---|---|
| | yield (in %) | | | percent conversion | yield (in %) | | | percent conversion |
| | aldehyde | ester | acid | | aldehyde | ester | acid | |
| 1 | 35.8 | 32.1 | 0.8 | 68.7 | 35.0 | 35.0 | 2.9 | 72.9 |
| 3 | 38.0 | 25.9 | 0.8 | 64.7 | 32.8 | 37.8 | 1.9 | 72.5 |
| 5 | 41.3 | 23.0 | 0.9 | 65.2 | 33.3 | 37.8 | 1.8 | 72.9 |
| 6 | 42.0 | 22.0 | 0.7 | 64.7 | 33.6 | 38.4 | 1.9 | 73.9 |
| 7 | 43.1 | 20.9 | 0.7 | 64.7 | 33.0 | 38.8 | 1.7 | 72.5 |
| 9 | 43.8 | 20.3 | 0.6 | 64.7 | 32.6 | 38.4 | 1.6 | 72.6 |
| 11 | 45.3 | 19.0 | 0.5 | 64.8 | 32.9 | 37.0 | 1.8 | 71.7 |
| 12 | 45.8 | 18.7 | 0.5 | 65.0 | 33.0 | 36.0 | 2.1 | 71.1 |
| 15 | 46.9 | 18.0 | 0.6 | 65.5 | 34.0 | 36.7 | 1.6 | 72.3 |

hydrogen at 200° until water ceased to evolve. Then the temperature was raised to the desired experimental temperature, and the addition of hydrogen was terminated if the experiment was run in the absence of hydrogen. The time of each experiment ranged from 10-30 hrs. Samples of the catalyzate were removed during experiment (at intervals of 1.5-2 hrs), and were analyzed separately.

The liquid products were analyzed by conventional methods. In addition, the catalyzate was subjected to fractional distillation through a column with an efficiency of 18 theoretical plates. The reaction products were identified by their physical constants and by elemental analysis of the corresponding derivatives.

As an example we present the results of the experiments run at 310° in the presence of nitrogen and of hydrogen, with a constant space velocity of 160 (Table 2).

## SUMMARY

1. The catalytic conversion of butyl alcohol over a copper catalyst was studied in the temperature range 250-370°, with dilution of the starting alcohol by various inert gases.

2. It was shown that the catalyst is deactivated during experiment due to the formation of difficultly desorbed products on its surface. The deactivation process can be retarded by the addition of gas diluents (nitrogen, hydrogen, carbon dioxide) to the starting alcohol. At high temperatures the nature of the gas diluent is not important. At lower temperatures (310°) a specific favorable influence is exerted by hydrogen on the retention of catalyst activity.

3. The functions of the catalyst change during the poisoning process, which is associated with the different orders of the reactions that progress on the catalyst surface.

4. An explanation of the observed rules was proposed.

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# SOME N-ω-PHENYLALKYL-β-CHLOROPROPIONAMIDES

## N. K. Kochetkov and N. V. Dubykina

In previous papers we have described the synthesis of a number of N-substituted β-chloropropionamides, containing benzyl and certain other radicals on the nitrogens [1, 2]. It was found that some of the obtained compounds are highly active anticonvulsants. It was also found that N-β-phenethyl-β-chloropropionamide (phenacon) is especially active in the treatment of tremors, in contrast to N-benzyl-β-chloropropionamide (chloracon), which is most active in the treatment of epileptic fits [3, 4].

In view of such a shift in the character of the anticonvulsant activity it seemed of interest to follow the effect of further lengthening of the alkyl chain separating the phenyl radical from the amido nitrogen on the physiological activity of N-substituted β-chloropropionamides.

With this in mind we synthesized the corresponding N-ω-phenylalkyl-β-chloropropionamides, and specifically: N-ω-phenylpropyl-β-chloropropionamide, N-ω-phenylbutyl-β-chloropropionamide and N-ω-phenylamyl-β-chloropropionamide. To determine the effect of other structural changes in the amide portion of the molecule we also synthesized N-phenylbutenyl-β-chloropropionamide and some other compounds.

All of the indicated compounds were synthesized by the scheme described by us earlier [1, 2], and specifically by the acylation of the corresponding amines with β-chloropropionyl chloride

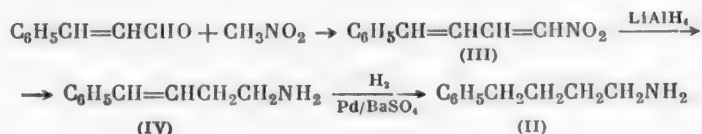$$RNH_2 + ClCOCH_2CH_2Cl \rightarrow RNHCOCH_2CH_2Cl$$

In the present paper we used a modified method and ran the acylation in a two-phase system by adding the acid chloride to a mixture composed of an ethyl acetate solution of the proper amine and an aqueous solution of sodium hydroxide. This permitted us to avoid a number of complications, and primarily a saponification of the acid chloride, which we observed when operating in an aqueous medium. With the indicated procedure the β-chloropropionamides were obtained in yields of 80-95%.

We used various methods to obtain the amines. ω-Phenylpropionamide (I) was obtained by hydrogenating the readily available β-phenylpropionitrile over skeletal nickel.

$$C_6H_6 + CH_2{=}CHCN \rightarrow C_6H_5CH_2CH_2CN \xrightarrow{H_2}{Ni} C_6H_5CH_2CH_2CH_2NH_2$$
$$(I)$$

To synthesize δ-phenylbutylamine (II) we used the following scheme:

$$C_6H_5CH{=}CHCHO + CH_3NO_2 \rightarrow C_6H_5CH{=}CHCH{=}CHNO_2 \xrightarrow{LiAlH_4}$$
$$(III)$$

$$\rightarrow C_6H_5CH{=}CHCH_2CH_2NH_2 \xrightarrow{H_2}{Pd/BaSO_4} C_6H_5CH_2CH_2CH_2CH_2NH_2$$
$$(IV) \qquad\qquad (II)$$

The condensation of cinnamaldehyde with nitromethane in the presence of alcoholic caustic gave 1-phenyl-4-nitrobutadiene (III). The direct catalytic hydrogenation of the latter failed to yield (II), since here the process was accompanied by the formation of high-boiling products, which is probably linked with the condensations suf-

fered by the nitrodiene under the hydrogenation conditions. Because of this we first reduced the nitrodiene (III) with aluminum lithium hydride, and the resulting δ -phenylbutenylamine (IV) was then converted to the unsaturated amine (II) by hydrogenation over palladium deposited on barium sulfate. The unsaturated amine (IV), obtained as an intermediate, was also used by us to obtain the corresponding N-substituted β -chloropropionamide for the purpose of determining the effect of a double bond in the alkyl chain on the physiological activity. The position of the double bond in the obtained δ -phenylbutenylamine cannot be considered as being rigidly established, but it is well known that when α,β -unsaturated nitro compounds are reduced with alumium lithium hydride it is the adjacent double bond that is reduced simultaneously with the nitro group [5, 6]. For this reason we believe that in the compound obtained by us it is the double bond in conjugation with the benzene ring that is retained, and therefore, the compound is 4-phenyl-3-butenylamine. The catalytic hydrogenation of the unsaturated β -chloro-propionamide gave N-ω-phenylbutyl- β -chloropropionamide, completely identical with the product obtained by direct hydrogenation.
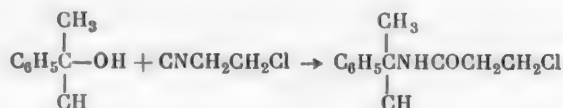
ω-Phenylamylamine (V) was synthesized by the following scheme:

$$C_6H_5CH{=}CHCHO + CH_2(COOH)_2 \rightarrow C_6H_5CH{=}CHCH{=}CHCOOH \xrightarrow{H_2}{Ni}$$
$$(VI)$$

$$\rightarrow C_6H_5(CH_2)_4COOH \rightarrow C_6H_5(CH_2)_4CONH_2 \xrightarrow{LiAlH_4} C_6H_5(CH_2)_5NH_2$$
$$(VII) \qquad\qquad (VIII) \qquad\qquad\qquad (V)$$
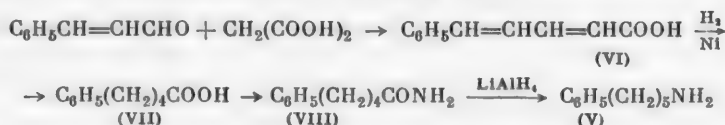
β -Styrylacrylic acid (VI), obtained by the condensation of cinnamaldehyde with malonic acid, was hydrogenated over nickel. The obtained ω-phenylvaleric acid (VII) was converted to the amide (VIII) via the corresponding acid chloride, which was not isolated. The reduction of the amide with lithium aluminum hydride led to obtaining (V) in a high yield.

In order to determine the effect of an additional phenyl radical in the amide portion of the molecule we synthesized N-β ,β -diphenylethyl-β -chloropropionamide. The β ,β -diphenylethylamine needed for this synthesis was obtained by the hydrogenation of diphenylacetonitrile, using the method recently described by one of us with M. I. Petruchenko [7].

Finally, to determine the effect of branching in the N-alkyl radical of the β -chloropropionamide, we synthesized N-α-phenylisopropyl- β -chloropropionamide. We used the Ritter reaction [8] to synthesize this compound, and the N-substituted β -chloropropionamide was obtained by reacting dimethylphenylcarbinol with β -chloropropionitrile.

$$\begin{array}{ccc} CH_3 & & CH_3 \\ | & & | \\ C_6H_5C{-}OH + CNCH_2CH_2Cl \rightarrow & C_6H_5CNHCOCH_2CH_2Cl \\ | & & | \\ CH & & CH \end{array}$$

The use of β -chloropropionitrile in the Ritter reaction was previously unknown, and although the amide in which we were interested was obtained in very small yield here, still the method possesses definite advantages due to the simplicity and ready availability of the starting materials. The complications associated with the instability of β -chloropropionitrile under the conditions of the Ritter reaction are the reason for the low yield of the amide.

All of the synthesized N-substituted β -chloropropionamides were tested in the Pharmacological Section of our Institute by N. V. Kaverina. Of the synthesized compounds only the three saturated derivatives of N- ω-phenyl- β -chloropropionamide (Table, compounds 1, 2 and 4) show some activity in the treatment of convulsions produced by arecoline. Consequently, N-benzyl-β -chloropropionamide and N-β -phenylethyl-β -chloropropionamide, synthesized by us earlier, possess the optimum anticonvulsant activity.

## EXPERIMENTAL

ω-Phenylpropylamine (I). Hydrocinnamonitrile was obtained by the literature method [9] in a yield of 60%; b. p. 100-102° (5 mm), $n^{19}D$ 1.5245.

A solution of 31.5 g of the nitrile in 100 ml of alcohol was hydrogenated in the presence of 15 g of skeletal nickel, and after the usual workup, we obtained 20.6 g (63.2%) of (I) with b. p. 78-80° (3 mm), $n^{20}D$ 1.5230.

Found %: N 9.88, 9.77. $C_9H_{13}N$. Calculated %: N 10.35.

The amine is a colorless liquid that avidly absorbs carbon dioxide from the air. From [10], b. p. 216-220°.

$\omega$-Phenylbutylamine (II). 1-Phenyl-4-nitrobutadiene (III). A solution of 6.3 g of sodium hydroxide in 60 ml of methanol was added in drops, with vigorous stirring and cooling to 0°, to a solution of 20 g of freshly distilled cinnamaldehyde and 9.3 g of nitromethane in 75 ml of methanol. The reaction mixture was stirred for another 20 min at 0-5°, the precipitate of (III) sodium salt filtered, then washed with cold methanol, and finally it was suspended in a large volume of ice water and the suspension poured into 160 ml of 1 N hydrochloric acid, cooled to 0°. The crystalline precipitate of (III) was filtered, washed with cold water, dried in the air, and re-crystallized from methanol. Yield 17.5 g (66%); yellow leaflets with m. p. 45-46°.

Found %: N 8.47, 8.26. $C_{10}H_9O_2N$. Calculated %: N 8.00.

4-Phenyl-3-butenylamine (IV). A solution of 12.8 g of (III) in 100 ml of ether was added with stirring and slight warming to an ether solution of lithium aluminum hydride (from 12.6 g of lithium hydride and 102 g of aluminum bromide in 260 ml of absolute ether), after which the mixture was heated under reflux for 4 hrs, stirred at room temperature for 5 hrs, and the excess aluminum hydride decomposed by the addition of 100 ml of moist ether, and then 20 ml of water. After this the reaction mixture was slowly poured with stirring into 10% hydrochloric acid (200 ml), cooled to 0°. The ether layer was separated and the water layer was first treated with excess concentrated caustic and then extracted with ether. The combined extracts were dried over sodium hydroxide, after which fractional distillation gave 10.5 g (77%) of (IV) with b. p. 90-91° (3.5 mm), $n_D^{27.5}$ 1.5548.

Found %: N 9.38, 9.67. $C_{10}H_{13}N$. Calculated %: N 9.52.

The compound is a colorless oil that instantly decolorizes permanganate solution.

The hydrochloride was obtained by saturating an ether solution of (IV) with dry hydrogen chloride. Colorless lustrous crystals with m. p. 219-221° (precipitation from methanol solution with ether).

Found %: Cl 19.48, 19.44. $C_{10}H_{14}NCl$. Calculated %: Cl 19.32.

The picrate was obtained in methanol solution; fine yellow crystals with m. p. 148-149° (from ether).

$\omega$-Phenylbutylamine (II). A solution of 0.9 g of (IV) in 50 ml of anhydrous methanol was hydrogenated in the presence of 0.3 g of palladium-on-barium sulfate (5% palladium) at room temperature. The amount of hydrogen absorbed was 130 ml (0°, 760 mm); theory is 122 ml. After the usual workup we obtained 0.63 g (70%) of (II) with b. p. 87-88° (3.5 mm), $n_D^{20}$ 1.5200.

The compound is an oil with a slight odor which slowly absorbs carbon dioxide from the air.

Found %: N 9.12, 8.97. $C_{10}H_{15}N$. Calculated %: N 9.39.

From [11], b. p. 123-124° (17 mm).

The hydrochloride was obtained in conventional manner; colorless lustrous crystals with m. p. 162-163°.

Found %: Cl 18.90, 18.86. $C_{10}H_{16}NCl$. Calculated %: Cl 19.11.

Picrate: m. p. 120-124° (from anhydrous alcohol).

$\omega$-Phenylamylamine (V). $\omega$-Phenylvaleric acid (VII). 5 g of styrylacrylic acid, obtained by the Doebner method [12], was hydrogenated in 100 ml of anhydrous alcohol in the presence of 3 g of skeletal nickel at atmospheric pressure and room temperature. The hydrogenation was stopped after 1.470 ml of hydrogen had been absorbed, the catalyst removed by filtration, and after distilling off the alcohol we obtained 5.1 g (100%) of (VII) as colorless crystals with m. p. 57.5-58.5°. From [13], m. p. 58-59°.

$\omega$-Phenylvaleramide (VIII). A mixture of 5 g of (VII) with 3.5 ml of thionyl chloride was heated on the water bath for 1 hr, then allowed to stand overnight, the excess thionyl chloride distilled off , and the residue poured into 20% aqueous ammonia solution; the obtained colorless crystals of (VIII) were filtered. Yield 4.0 g (80%); m. p. 104-106°. From [14], m. p. 104-105°.

$\omega$-Phenylamylamine (V). A suspension of 10.2 g of (VIII) in 200 ml of ether was added to a solution of 607 g of aluminum lithium hydride in 400 ml ether in 1 hr, the mixture stirred for another hour, and then the

reaction was worked up as described above. Fractional distillation gave 4.5 (80%) of (V) with b. p. 88-89° (4 mm), $n^{20}D$ 1.5310.

Found %: N 8.32, 8.27. $C_{11}H_{17}N$. Calculated %: N 8.58. From [11], b. p. 131° (15 mm).

The amine is an oil with a slight odor which slowly absorbs carbon dioxide from the air.

The hydrochloride was obtained in conventional manner; colorless glistening leaflets with m. p. 150-151° (precipitation from methanol solution with ether).

Found %: Cl 17.75, 17.78. $C_{11}H_{18}NCl$. Calculation %: Cl 17.77.

N-Substituted-β-chloropropionamides. β-Chloropropionyl chloride (0.13 mole) was slowly added, with vigorous stirring and cooling to 0-5°, to a mixture of 0.13 mole of the amine in 100 ml of ethyl acetate and a solution of 5.3 g of sodium hydroxide in 50 ml of water. Then the pH of the mixture was adjusted to 7.5-8.0 by the addition of a small amount of caustic, and the stirring continued for another 30-40 min at room temperature. The ethyl acetate layer was separated, washed with water until neutral, then dried over sodium sulfate, the solvent vacuum-distilled, and the crystalline residue recrystallized from either alcohol or petroleum ether. The data on the compounds obtained by the described method are summarized in the table.

N-Substituted β-Chloropropionamides ($RNHCOCH_2CH_2Cl$)

| Expt. no. | R | Yield (in %) | Melting point | Amount in % | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | C | | H | | N | | Cl | |
| | | | | found | calc. | found | calc. | found | calc. | found | calc. |
| 1 | $C_6H_5CH_2CH_2CH_2$ | 89 | 55—57° from alcohol | 63.98, 64.01 | 63.88 | 7.33, 7.42 | 7.09 | 6.03, 6.13 | 6.20 | 15.52, 15.50 | 15.71 |
| 2 | $C_6H_5CH_2CH_2CH_2CH_2$ | 87 | 45—46 from petroleum ether | — | — | — | — | 6.16, 6.10 | 5.84 | 14.49, 14.76 | 14.79 |
| 3 | $C_6H_5CH=CHCH_2CH_2$ | 77 | 95.5—100.5 from alcohol | — | — | — | — | 5.79, 5.66 | 5.86 | 15.05, 14.79 | 14.92 |
| 4 | $C_6H_5CH_2CH_2CH_2CH_2CH_2$ | 95 | 56—57 from petroleum ether | 66.30, 66.34 | 66.30 | 8.00, 7.86 | 7.88 | 5.80, 5.77 | 5.52 | 14.08, 14.11 | 13.97 |
| 5 | $(C_6H_5)_2CHCH_2$ | 90 | 112—113.5 from alcohol | — | — | — | — | 4.85, 4.62 | 4.86 | 12.41, 12.54 | 12.36 |

Hydrogenation of N-ω-phenylbutenyl-β-chloropropionamide. A solution of 0.5 g of the compound in 10 ml of alcohol was hydrogenated in the presence of 0.2 g of palladium-on-barium sulfate at atmospheric pressure and room temperature. The hydrogenation was stopped after the theoretical amount of hydrogen had been absorbed, and the usual workup gave 0.45 g (90%) of N-ω-phenylbutyl-β-chloropropionamide. Recrystallization from alcohol gave the compound as colorless crystals with m. p. 44-45°. The melting point was not depressed when the compound was mixed with the compound obtained by the acylation of δ-phenylbutylamine.

N-δ-Phenylisopropyl-β-chloropropionamide. To a solution of 16.2 g of dimethylphenylcarbinol and 10.5 g of β-chloropropionitrile in 30 ml of glacial acetic acid, with stirring and cooling, was slowly added 6 ml of concentrated sulfuric acid, and then the mixture was allowed to stand overnight. The two-layer reaction mixture was poured into 500 ml of water, the acid neutralized with soda, the product extracted with ether, the ether extracts dried over magnesium sulfate, and the ether removed by distillation. The residue was distilled at 0.1 mm, collecting the fraction with b. p. 80-110°, and contained a crystalline product as impurity; the latter was removed by adding petroleum ether to the distillate; yield 1.2 g (5%). Colorless glistening crystals with m. p. 90-91° (from alcohol).

Found %: N 6.10, 6.17; Cl 15.78, 15.85. $C_{12}H_{16}ONCl$. Calculated %: N 6.26; Cl 15.71.

## SUMMARY

Some N-$\omega$-phenylalkyl-$\beta$-chloropropionamides and related compounds were synthesized, and their pharmacological activity was investigated. The acylation of the arylalkylamines with $\beta$-chloropropionyl chloride was run in a two-phase system (ethyl acetate-water) in the presence of sodium hydroxide.

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* Original Russian pagination. See C. B. translation.

# REACTION OF p-HALOPHENYLHYDRAZINES WITH ARSENIC ACID

O. A. Zeide, S. M. Sherlin, and A. B. Bruker

Earlier it had been shown that the reaction of arsenic acid with phenylhydrazine (in aqueous solution), depending on the experimental conditions, gives in good yields phenylarsine oxide, diphenylarsine oxide and triphenylarsine oxide, provided the reaction is run in the presence of copper or its salts [1].

It seemed of interest to us to determine to what extent this reaction is general for the preparation of other substituted arylarsine oxides. To answer this we decided to investigate the possibility of forming arylarsine oxides with halogen atoms in the para-position to the arsenic radical. For this purpose we reacted p-chloro-, p-bromo- and p-fluorophenylhydrazine with arsenic acid.

The proper hydrazine was gradually added with stirring to a heated water solution of arsenic acid, to which copper bronze had been previously added.

It proved that both p-chloro- and p-bromophenylhydrazine react in normal manner, similar to phenyl- and tolylhydrazine, and give the corresponding substituted arylarsine oxides as the final product. After the workup, described in detail in the Experimental section, we isolated (p-chlorophenyl) dichloroarsine and chlorodi-(p-chlorophenyl) arsine. In the reaction with the bromophenylhydrazine we isolated chlorodi-(p-bromophenyl) arsine, which in turn was converted to the corresponding acid by oxidation with hydrogen peroxide.

With this method we were also able to obtain chlorodi-(p-fluorophenyl) arsine from p-fluorophenylhydrazine, which on subsequent oxidation was converted to the corresponding di-(p-fluorophenyl) arsenic acid.

Mention should be made of some of the properties of the fluoro-substituted aromatic arsenic compounds. Thus, chlorodi-(p-fluorophenyl) arsine is much more difficult to oxidize than the corresponding chlorophenyl and bromophenyl derivatives.

Hydrogen peroxide is a poor oxidizing agent here, and we were able to obtain much better results by using nitric acid (d 1.4) as the oxidizing agent.

It is interesting to mention that the constants of the p-fluoro derivatives of arylarsenic compounds prove to be very close to the corresponding constants of the phenyl derivatives of arsenic.

## EXPERIMENTAL

<u>Oxidation of p-chlorophenylhydrazine with arsenic acid.</u> To a solution of 70 g of arsenic acid in 210 ml of water, heated to 70°, to which 3 g of copper bronze had been previously added, was gradually added with good stirring 40 g of p-chlorophenylhydrazine. The reaction was ended in 2 hrs, and here a heavy oil collected on the bottom of the flask. The water layer was decanted from the oil, and the oil was shaken with fuming hydrochloric acid to convert the arsenic oxides to the chlorides. The (p-chlorophenyl) dichloroarsine and chlorodi-(p-chloro-phenyl) arsine obtained here were then fractionally distilled.

Two fractions were collected: 1st, 160-170° (20 mm), 6 g, and 2nd, 180-240° (20 mm) (main portion distilled at 225°), 17 g. At atmospheric pressure the 1st fraction distilled mainly at 277°, which corresponds to the boiling point of (p-chlorophenyl) dichloroarsine. For further identification the chloride was hydrolyzed with aqueous ammonia solution. The thus obtained oxide after recrystallization from benzene had m. p. 184°, which corresponds to the melting point of p-chlorophenylarsine oxide. The 2nd fraction was redistilled and boiled at

225° (15 mm). The distillate on cooling solidified to a crystalline mass with m. p. 51° (from the literature [4], m. p. 51°).

Oxidation of p-bromophenylhydrazine with arsenic acid. The experiment was run using the conditions described above. The following fractions were collected: 1st, 117-130° (0.4-0.8 mm), 7.8 g, and 2nd, 138-165° (0.4-0.8 mm), 9.0 g.

To effect a better separation of the primary and secondary arsenic compounds, both fractions were oxidized with hydrogen peroxide and converted to the corresponding acids. After recrystallization of the products of the oxidation of the 1st fraction from alcohol we obtained colorless crystals of p-bromophenylarsenic acid, which proved to be difficultly soluble in water, alcohol and other organic solvents, and did not melt when heated to 280°. The oxidation product of the 2nd fraction proved to be di-(p-bromophenyl)arsenic acid. It crystallizes from boiling alcohol as colorless prisms (m. p. 186-187°), and is very difficultly soluble in water, acetone, chloroform and petroleum ether.

Found %: As 17.80. $C_{12}H_9O_2Br_2As$. Calculated %: As 17.86.

To obtain the pure chloride we took the di-(p-bromophenyl)arsenic acid and converted it to the chloride by reduction with sulfur dioxide in concentrated hydrochloric acid in the presence of potassium iodide. The obtained oil solidified and was recrystallized from alcohol. The chloride was obtained as well-shaped crystals with m. p. 57-58°.

Found %: As 17.50. $C_{12}H_8ClBr_2As$. Calculated %: As 17.75.

Oxidation of p-fluorophenylhydrazine with arsenic acid. The starting product for the preparation of p-fluoro-phenylhydrazine was p-fluoronitrobenzene, which we obtained by reacting a concentrated solution of p-nitroben-zenediazonium sulfate with concentrated hydrofluoric acid at the boil [2]. However, the conditions for the diazotization of p-nitroaniline, recommended by Holleman and Beekman to obtain a concentrated solution of the diazonium sulfate, give much difficulty in that each drop of the nitrite causes a slight explosion. Consequently, we were forced to run the diazotization in less concentrated media, which proved to be more practical. The fluoro-nitrobenzene was converted to the fluorophenylhydrazine through p-fluoroaniline [3]. Then 31 g of p-fluoro-phenylhydrazine was oxidized with a hot solution of 71 g of arsenic acid in 213 ml of water under the conditions described in the preceding experiment. The obtained organoarsenic oxides were then converted to the chlorides, and after the usual workup, the lattter were fractionally distilled at 12 mm, where the following fractions were collected: 1st, 132-150° (mostly at 140-145°), 4 g; 2nd, 160-170° (mostly at 162-164°), 12 g; and 3rd, 170-176°, 5.2 g.

To obtain complete separation, the different chloride fractions were converted to the acids. Very little reaction occurred when we attempted to oxidize the 2nd fraction with hydrogen peroxide; vigorous reaction occurred when we used nitric acid (d 1.4) and a solid product was formed. Recrystallization of the solid from a large volume of boiling water gave long colorless prismatic crystals with m. p. 136-138°. The compound is very difficultly soluble in cold water, and readily soluble in hot alcohol.

Based on the analysis data, the compound proved to be di-(p-fluorophenyl)arsonic acid.

Found %: As 24.80. $C_{12}H_9O_2F_2As$. Calculated %: As 25.17.

To obtain chlorodi-(p-fluorophenyl)arsine the recrystallized acid was converted to the chloride by reduction with sulfur dioxide in strong hydrochloric acid. The obtained oil distilled at 156-157° at 13 mm. On cooling the oil solidified and after recrystallization from alcohol was obtained as colorless crystals with m. p. 39°.

Found %: Cl 11.86. $C_{12}H_8F_2ClAs$. Calculated %: Cl 11.76.

## SUMMARY

On the examples of p-Br-, p-Cl- and p-F-phenylhydrazines it was shown that the preparation of organo-arsenic compounds from arylhydrazines and arsenic acid in the presence of metallic copper is a general reaction.

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# NEW METHOD FOR THE PREPARATION OF ORGANOARSENIC COMPOUNDS BY THE OXIDATION OF A MIXTURE OF PHENYLHYDRAZINE AND ARSENIC TRICHLORIDE WITH ATMOSPHERIC OXYGEN IN THE PRESENCE OF CUPRIC CHLORIDE

A. B. Bruker and N. M. Nikiforova

Wieland and Madelung [1], in oxidizing phenylhydrazine with phenylarsenic and diphenylarsenic acid, obtained triphenylarsine. Attempts to isolate organoarsenic compounds when phenylhydrazine was oxidized with arsenic acid proved unsuccessful.

Zeide, Sherlin and Bras [2], on reacting phenyl- or tolylhydrazine in aqueous solution with arsenic acid in the presence of copper or its salts, obtained a mixture of phenyl- or tolylarsine oxide, diphenyl- or ditolylarsine oxide and triphenyl- or tritolylarsine. This same method was also used to obtain the p-chloro-, p-bromo- and p-fluorophenylarsenic compounds [3].

In a paper by Bruker and Makliaev [4] on the role of copper in obtaining aromatometallic compounds by either the diazo or hydrazino reaction it was shown that if an inorganic arsenic compound is the starting product, then to obtain aromatoarsenic componds it is necessary to have copper present. If it is aromatic arsenic compounds that are subjected to arylation, then this reaction also goes in the absence of a special catalyst. Consequently, the difference between the reaction of Zeide, Sherlin and Bras and that of Wieland and Madelung consists only in the use of copper or its salts as catalyst.

In previous papers we have described a new method for the preparation of aromatic compounds of antimony, consisting in the reaction of an arylhydrazine with antimony trichloride [5] or with antimony pentachloride [6] in hydrochloric acid medium in the presence of cupric chloride, in which connection atmospheric oxygen is the oxidizing agent in this reaction.

In the present paper our goal was to investigate the possibility of obtaining aromatoarsenic compounds by the same method that we used earlier to synthesize aromatoantimony compounds. Actually, when phenylhydrazine hydrochloride (1 mole) was reacted with arsenic trichloride (1 mole) in hydrochloric acid medium in the presence of cupric chloride and atmospheric oxygen we obtained phenyldichloroarsine in 58-65% yield (based on arsenic trichloride).

The formation of phenyldichloroarsine in this reaction can be depicted as follows: phenylhydrazine hydrochloride is oxidized by atmospheric oxygen in the presence of cupric chloride to benzenediazonium chloride, and the latter then reacts with arsenic trichloride to give the intermediate binary compound.
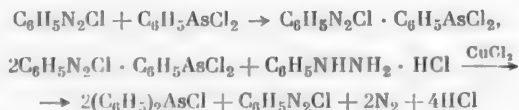
$$C_6H_5NHNH_2 \cdot HCl + AsCl_3 + O_2 \xrightarrow{CuCl_2} C_6H_5N_2Cl \cdot AsCl_3 + 2H_2O$$
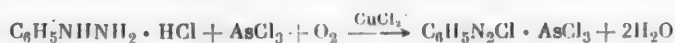
A second molecule of phenylhydrazine reduces the binary compound to phenyldichloroarsine, and is itself oxidized to benzenediazonium chloride.

$$2C_6H_5N_2Cl \cdot AsCl_3 + C_6H_5NHNH_2 \cdot HCl \xrightarrow{CuCl_2} 2C_6H_5AsCl_2 + C_6H_5N_2Cl + 2N_2 + 4HCl$$

The following facts serve as proof of this. Phenyldichloroarsine is formed when phenylhydrazine hydrochloride is reacted under the above-described conditions with the binary compound $C_6H_5N_2Cl \cdot AsCl_3$, obtained directly from benzenediazonium chloride and arsenic trichloride. As regards the indicated intermediate binary compound, then we found it impossible to isolate it from the reaction mixture obtained in the reaction with phenylhydrazine. However, as evidence that it is formed is the fact that the binary compound $C_{10}H_7N_2Cl \cdot AsCl_3$ is obtained when β-naphthylhydrazine is reacted with $AsCl_3$ under similar conditions.

Together with phenyldichloroarsine, diphenylchloroarsine is formed in the reaction of arsenic trichloride with phenylhydrazine and benzenediazonium chloride.

The formation of diphenylchloroarsine in this reaction is apparently due to the fact that phenyldichloroarsine, partially dissolving in the aqueous hydrochloric acid reaction solution, gives the binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$ with benzenediazonium chloride, which is then reduced by phenylhydrazine to diphenylchloroarsine.

$$C_6H_5N_2Cl + C_6H_5AsCl_2 \rightarrow C_6H_5N_2Cl \cdot C_6H_5AsCl_2,$$
$$2C_6H_5N_2Cl \cdot C_6H_5AsCl_2 + C_6H_5NHNH_2 \cdot HCl \xrightarrow{CuCl_2}$$
$$\rightarrow 2(C_6H_5)_2AsCl + C_6H_5N_2Cl + 2N_2 + 4HCl$$

It could be postulated that if the reaction was run in alcoholic hydrochloric acid medium, in which phenyldichloroarsine is much more soluble than in aqueous hydrochloric acid solution, then the yield of diphenylchloroarsine should increase due to the fact that here more favorable conditions exist for the formation of the binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$.

Actually, a mixture of phenyldichloroarsine and diphenylchloroarsine, with a predominance of the diphenylchloroarsine, is formed when phenylhydrazine hydrochloride (2.2 moles) is reacted with arsenic trichloride (1 mole), or when a mixture of phenylhydrazine hydrochloride and benzenediazonium chloride is reacted with arsenic trichloride, in alcoholic hydrochloric acid medium in the presence of cupric chloride and atmospheric oxygen.

The results of our experiments, in which the reaction of benzenediazonium chloride with phenyldichloroarsine in alcoholic hydrochloric acid medium gave the binary compound of benzenediazonium chloride and phenyldichloroarsine $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$, from which secondary aromatoarsenic compounds are subsequently formed, can serve as evidence that the formation of secondary aromatoarsenic compounds goes through the binary compound of type $ArN_2Cl \cdot ArAsCl_2$.

Since diphenylchloroarsine is practically insoluble in alcohol hydrochloric acid medium, it fails to react with benzenediazonium chloride to give the binary compound $(C_6H_5)_2AsCl \cdot C_6H_5N_2Cl$, from which it is possible to obtain tertiary arsines. This is probably the reason why we were unable to find any tertiary arsines in the reaction mass when using our method.

Consequently, the mechanism proposed by us earlier for the formation of aromatic compounds of arsenic and antimony via the diazo reaction [7] is again confirmed in the present study.

## EXPERIMENTAL

I. Reaction of arsenic trichloride with phenylhydrazine in hydrochloric acid medium in the presence of catalysts and atmospheric oxygen. Into a 500-ml flask, fitted with seal-stirrer, two spargers and a reflux condenser, was charged arsenic trichloride (18 g), hydrochloric acid (80 ml, d 1.19), phenylhydrazine (11 g), water (225 ml) and catalysts (0.5 g of cupric chloride and 3 g of ferric chloride). The stirrer was turned on, and the top of the reflux condenser was connected to a water-jet pump to suck air through the reaction mixture. The heavy oil that separated after stirring for 36 hrs was separated from the liquid. The crude phenyldichloroarsine weighed 15 g (65.5%, based on arsenic trichloride). Vacuum-distillation gave 13 g (58%, based on arsenic trichloride) of phenyldichloroarsine with b. p. 116° (6 mm).

II. Preparation of binary compound of β-naphthalenediazonium chloride with arsenic trichloride from β-naphthylhydrazine hydrochloride and arsenic trichloride in hydrochloric acid medium. To a solution of 6.6 g of arsenic trichloride in 100 ml of hydrochloric acid (d 1.19) was added 0.5 g of cupric chloride and 0.5 g of ferric

chloride. When the arsenic trichloride, cupric chloride and ferric chloride had dissolved, 4 g of β-naphthylhydrazine hydrochloride was added in small portions and with good stirring. After stirring for an hour a test with β-naphthol gave the diazo reaction. The stirring was continued for 45 hrs. The obtained yellow-green precipitate was suction-filtered, and then washed with hydrochloric acid (d 1.19) and absolute ether. Yield 7.2 g (64%, based on arsenic trichloride).

Found %: As 19.81, 19.35; N 6.92, 7.21; Cl 38.05, 38.93. $C_{10}H_7Cl_4N_2As$. Calculated %: As 20.17; N 7.53; Cl 38.70.

Decomposition of the binary compound with dilute ammonia solution gave β-naphthylarsenic acid (yield about 50%), which when reduced with $SO_2$ in hydrochloric acid medium gave β-naphthyldichloroarsine with m. p. 67-68°.

III. Preparation of a mixture of phenyldichloroarsine and diphenylchloroarsine. a) Preparation of binary compound $C_6H_5N_2Cl \cdot AsCl_3$. * Arsenic trichloride (36.6 g) was added with stirring to a solution of 25.9 g of aniline hydrochloride in 130 ml of anhydrous alcohol. The obtained mixture was diazotized under cooling (1-3°) with isoamyl nitrite (23.3 g). The reaction was run in a closed vessel, fitted with a mercury-seal stirrer, dropping funnel and reflux condenser. After diazotization the reaction mass was stirred for 10 min. Then the filtrate was removed by rapid suction-filtration, while the precipitate was washed several times with absolute ether and then dried in a desiccator over sulfuric acid. The yield of product was 44.1 g (65% based on arsenic trichloride).

Found %: As 23.02, 22.55; N 8.63, 8.55. $C_6H_5Cl_4N_2As$. Calculated %: As 23.29; N 8.70.

The compound was obtained as a white crystalline powder, which soon turned yellow. It gives the diazo reaction with β-naphthol. On standing it suffers partial decomposition, accompanied by the formation of chlorobenzene. M. p. 83-85° (with decomp.). The compound is soluble in water, hydrochloric acid and alcohol, and insoluble in absolute ether. It decomposes with the evolution of nitrogen in the presence of copper in alcohol, acetone or glacial acetic acid, and also when heated with dilute hydrochloric acid or water.

b) Decomposition of the complex $C_6H_5N_2Cl \cdot AsCl_3$ in order to obtain aromatoarsenic compounds. A mixture of binary compound $C_6H_5N_2Cl \cdot AsCl_3$ (22 g) and cupric chloride (0.2 g) was dissolved in dilute hydrochloric acid (1 : 3) in an open flask with stirring. Then phenylhydrazine hydrochloride (9 g) was added to the solution and the reaction mass was stirred for 20 hrs. The oily product (14 g) was separated from the liquid. The oil was dissolved in hot alcohol (60 ml). The alcohol solution was then added to 125 ml of 5% ammonia, and the obtained mass of oxides, after separation from the liquid, was treated with hot concentrated hydrochloric acid (50 ml, d 1.19). The weight of the product after treatment was 8.7 g. Fractional distillation gave two fractions: 1st, phenyldichloroarsine, 127-129° (13 mm), 4.3 g; and 2nd, diphenylchloroarsine, 172-175° (11 mm), 4.2 g. The 2nd fraction crystallized when cooled and seeded. After recrystallization from alcohol the product had m. p. 38-39°. The yield of distilled diphenylchloroarsine was 25.6% (based on arsenic trichloride). The yield of distilled phenyldichloroarsine was 31.1% (based on arsenic trichloride).

IV. Reaction of arsenic trichloride, benzenediazonium chloride and phenylhydrazine hydrochloride in hydrochloric acid medium in the presence of catalysts. a) Preparation of the binary compound $C_6H_5N_2Cl \cdot AsCl_3$ and its solution. A solution of benzenediazonium chloride was added in drops to a mixture of arsenic trichloride (18.1 g) and hydrochloric acid (50 ml, d 1.19). The obtained precipitate of binary compound $C_6H_5N_2Cl \cdot AsCl_3$ was dissolved by the addition of dilute hydrochloric acid (200 ml).

b) Preparation of phenyldichloroarsine and diphenylchloroarsine. The solution obtained in a) was treated with 12 g of phenylhydrazine hydrochloride and 1 g of ferric chloride. Then a solution of 0.5 g of cupric chloride in 10 ml of hydrochloric acid (1 : 2) was added in 20 min. The reaction was run with cooling and stirring. After stirring for 12 hrs the oily product was separated from the liquid. The oil weighed 25 g. The oil was treated with 50 ml of benzene, and the benzene solution was dried over calcium chloride. After removal of the benzene by distillation the residue was vacuum-distilled: 1st fraction, phenyldichloroarsine, 130-135° (10-12 mm), 15.4 g; 2nd fraction, diphenylchloroarsine, 165-170° (10-12 mm), 3 g. The yield of distilled phenyldichloroarsine, based on arsenic trichloride, was 69.5%. The yield of diphenylchloroarsine was 11.3%.

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* Done jointly with N. M. Korneichuk.

V. Reaction of arsenic trichloride with phenylhydrazine hydrochloride in alcohol-hydrochloric acid medium in the presence of cupric chloride. The experiment was run using the same apparatus as in Expt. I. Into the reaction flask was charged water (150 ml), hydrochloric acid (50 ml, d 1.19), arsenic trichloride (18 g), phenylhydrazine hydrochloride (33 g), alcohol (200 ml) and cupric chloride (1 g). The reaction was run at 50° with the passage of air through the mixture. After stirring for 39 hrs the oily product was separated from the alcohol-hydrochloric acid solution. The crude product weighed 15 g. Vacuum-distillation gave two fractions: 1st (phenyldichloroarsine), 130° (10 mm), 3.3 g; 2nd (diphenylchloroarsine), 202-220° (16 mm), 7.3 g. The 2nd fraction crystallized on cooling, and the crystals melted at 36°. The yield of distilled phenyldichloroarsine, based on arsenic trichloride, was 14.8%. The yield of distilled diphenylchloroarsine, also based on arsenic trichloride, was 28%.

VI. Reaction of arsenic trichloride, benzenediazonium chloride and phenylhydrazine hydrochloride in the presence of catalysts. A mixture of arsenic trichloride (18.1 g) and hydrochloric acid (50 ml, d 1.19) was charged into a stoppered flask, fitted with a seal-stirrer and a wide tube for adding the reactants. The mixture was cooled to 2-3° and then a solution of benzenediazonium chloride, obtained by the diazotization of 9.3 g of aniline with a solution of 7.5 g of sodium nitrite in 13 ml of water and dilute hydrochloric acid (26 ml of hydrochloric acid and 30 ml of water), was added in drops with stirring. The formation of a precipitate was observed here, the color of which ranged from yellowish to pink.

Phenylhydrazine (12 g), methyl alcohol (250 ml) and ferric chloride (1 g) were then added to the reaction mixture. The reaction was run with cooling and stirring. A solution of cupric chloride (0.5 g in 10 ml of hydrochloric acid; 1 : 2) was added to the reaction mass in 15-20 min. After stirring for 6 hrs the oily product was separated from the liquid and washed several times with 2% hydrochloric acid. The crude product weighed 16.3 g. The product was treated with 50 ml of benzene, and the benzene solution was dried over calcium chloride. The benzene was distilled off and the residue was vacuum-distilled: 1st fraction, phenyldichloroarsine, 130-135° (10-15 mm), 1.8 g (8%, based on taken $AsCl_3$); 2nd fraction, diphenylchloroarsine, 178-182° (10-12 mm), 10.6 g (40%, based on taken $AsCl_3$).

VII. Reaction of benzenediazonium chloride and phenyldichloroarsine in alcoholic medium. * a) Preparation of binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$. Phenyldichloroarsine (16.5 g) was added with stirring to an alcohol solution of 6.5 g of aniline hydrochloride. The solution was cooled to 3° and then diazotized with 6.8 g of amyl nitrite. The obtained pink crystalline precipitate was suction-filtered rapidly, washed 3 times with absolute ether, and dried in a vacuum-desiccator. The obtained binary compound weighed 6.5 g. The odorless, cream-colored crystals partially decomposed on standing with the liberation of chlorobenzene. The binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$ is soluble in ethyl and methyl alcohols, and difficultly soluble in carbon tetrachloride, acetone and chloroform. M. p. 88-90° (with decomp.).

Found %: Cl 28.64, 29.02; As 19.23, 18.70; N 7.54, 8.31, 8.06. $C_{12}H_{10}Cl_3N_2As$. Calculated %: Cl 29.30; As 20.64; N 7.69.

b) Preparation of diphenylarsenic acid from binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$. The binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$ (1.6 g) was added gradually to a solution of 3 g of sodium bicarbonate in 100 ml of water. The reaction was accompanied by the evolution of nitrogen. On conclusion of reaction the solution was evaporated to a volume of 75 ml, filtered, and the filtrate acidified with hydrochloric acid. The obtained precipitate of diphenylarsenic acid weighed 0.65 g, and after recrystallization from water had m. p. 173°. Yield 56.5% (based on arsenic).

VIII. Preparation of diphenylchloroarsine from phenyldichloroarsine and benzenediazonium chloride without isolation of the binary compound $C_6H_5N_2Cl \cdot C_6H_5AsCl_2$. A solution of 8 g of aniline hydrochloride in 15 ml of hydrochloric acid (d 1.19) and 20 ml of ethyl alcohol was diazotized under cooling and stirring with a solution of 5 g of sodium nitrite in 10 ml of water. Then 12.4 g of phenyldichloroarsine, 0.3 g of copper sulfate and 2% sodium hydroxide solution was gradually added to the benzenediazonium chloride until the reaction was neutral. The evolution of nitrogen was observed here. Caustic was then added until the reaction was alkaline and after stirring for 12 hrs the mixture was filtered and the filtrate acidified with 5 N hydrochloric acid. The obtained precipitate of phenylarsenic acid was suction-filtered. Yield 8.5 g (61%). The acid was reduced with sulfur dioxide in hydrochloric acid medium (in the presence of KI). We obtained 7.12 g (48.5%) of diphenylchloroarsine with m. p. 36°.

* Done jointly with O. O. Kovtun.

IX. Reaction of binary compound $C_6H_5N_2Cl \cdot AsCl_3$ with phenylhydrazine hydrochloride in alcohol-hydrochloric acid medium in the presence of cupric chloride and ferric chloride. The reaction was run in the apparatus described in Expt. I. A solution of binary compound $C_6H_5N_2Cl \cdot AsCl_3$ (16 g), cupric chloride (0.5 g) and ferric chloride (1.5 g) in dilute hydrochloric acid (150 ml, 1 : 3) was prepared. Phenylhydrazine hydrochloride (7.2 g) was then gradually added to the obtained solution with stirring. The reaction mixture was stirred. Alcohol (150 ml) was gradually added through a dropping funnel. After vigorous stirring for 4 hrs the reaction mixture was allowed to stand overnight. The obtained oil was separated from the liquid. The crude product weighed 8.6 g. The product crystallized in a cooling mixture, but melted at room temperature. The crude product was dissolved in hot alcohol (60 ml) and then hydrolyzed with 5% ammonia (80 ml) with shaking. The obtained red mass of oxides was treated with 30% caustic (15 ml) with heating to 90°. The insoluble diphenylarsine oxide was separated, and then washed in the cold with 30% caustic and water. The yield of diphenylarsine oxide was 5 g (42.5%, based on $AsCl_3$).

From 5 g of $[(C_6H_5)_2As]_2O$ we obtained 3.6 g (27.5%, based on $AsCl_3$) of diphenylchloroarsine with m. p. 37°. Dilution of the alkaline filtrate with water, followed by acidification until weakly acid, gave 1.3 g (15.5%, based on inorganic arsenic) of phenylarsine oxide. From 1.3 g of $C_6H_5AsO$ we obtained 0.9 g (8.1%, based on consumed $AsCl_3$) of phenyldichloroarsine.

## SUMMARY

It was shown that the reaction of phenylhydrazine and arsenic trichloride in hydrochloric acid medium in the presence of cupric chloride and atmospheric oxygen yields primary and secondary aromatoarsenic compounds. A mechanism for the reaction was postulated and verified experimentally.

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# PREPARATION OF ESTERS OF FLUOROANTIMONIOUS AND FLUOROTITANIC ACIDS BY TREATMENT OF THE COMPLETE ESTERS OF THESE ACIDS WITH ANTIMONY TRIFLUORIDE

A. B. Bruker, R. I. Frenkel', and L. Z. Soborovskii

In the series of esters of titanic and antimonious acids, complete esters of these acids and certain chloro-, bromo-, and iodo-derivatives of titanium and antimony have been described. Alkoxy titanium fluorides and alkoxyfluorostibines have not been described up to now.

In the present work the reactions of antimony trifluoride with the complete esters of titanic and antimonious acids were studied; as we showed, they led to the formation of alkoxytitanium fluorides and alkoxyfluorostibines.

Similar reactions (the opposite of the disproportionation) have been widely used for the preparation of alkoxy-chloro-derivatives. In particular, the preparation of various alkoxytitanium chlorides through the reaction of titanium tetrachloride with alkyl orthotitanates has been described by A. N. Nesmeianov, R. Kh. Freidlina, and co-workers [1].

We found that in the reaction of antimony trifluoride with alkoxystibines, dialkoxyfluorostibines of the type $(RO)_2SbF$ (where $R = C_2H_5$, iso-$C_3H_7$) could be obtained in satisfactory yields. In this case it was established that double compounds having the hypothetical structure $Sb(OR)_3 \cdot 3Sb(OR)_2F$ can be isolated as intermediate products of this reaction; on subsequent heating in vacuo these compounds dissociate and give a dialkoxyfluorostibine and a trialkoxystibine, which are separated by distillation.

Thus on heating a mixture of triethoxystibine (3 moles) and antimony trifluoride (1 mole) to 150°, there was isolated a solid, homogeneous product melting at 56-59° and, according to analytical data, corresponding to the composition

$$SbF_3 \cdot 3Sb(OC_2H_5)_3 \tag{1}$$

However, a closer study of this product made it possible to propose a structure for it, corresponding to the double compound

$$Sb(OC_2H_5)_3 \cdot 3Sb(OC_2H_5)_2F \tag{2}$$

In particular, the fact that an identical compound is obtained in the reaction of 3 moles of diethoxyfluoro-stibine with 1 mole of triethoxystibine may serve as a certain confirmation. Besides this, it is possible that the formation of the indicated double compound (2) is the result of a secondary process and that complex (1) is first formed.

On distillation in vacuo of the double compound (2) or the reaction mixture obtained in the reaction of triethoxystibine and antimony trifluoride, diethoxyfluorostibine and triethoxystibine were isolated.

Diisopropoxyfluorostibine was prepared similarly. In this case the latter was separated with difficulty from triisopropoxystibine, which has nearly the same boiling point, on distillation of the reaction mixture in vacuo. The alkoxyfluoro-derivative was isolated from the distillate by freezing.

This method of preparing alkoxyfluoro-derivatives proved applicable also in those cases in which antimony trifluoride is made to react with alkoxy-derivatives of titanium. Thus, when antimony trifluoride was heated with various alkyl orthotitanates, the corresponding trialkoxytitanium fluorides were obtained. In this case double compounds of the type $Sb(OR)_3 \cdot 3Ti(OR)_3F$ (3) also were isolated as intermediate products of this reaction.

The reaction may be represented by the following scheme, from which it is evident that this process may be used both for the synthesis of alkoxytitanium fluorides and for the preparation of trialkoxystibines.

$$3Ti(OR)_4 + SbF_3 \rightarrow Sb(OR)_3 \cdot 3Ti(OR)_3F \rightarrow 3Ti(OR)_3F + Sb(OR)_3$$

Triethoxy-, triisopropoxy-, and tributoxytitanium fluorides were prepared in this way. The first two are crystalline substances; the last is a colorless liquid.

The intermediate double compounds (3) obtained from ethyl and isopropyl orthotitanates are solid substances, whereas that from butyl orthotitanate is a liquid.

In order to confirm that the compounds obtained were trialkoxytitanium fluorides, they were prepared also by treatment of the corresponding alkyl orthotitanates with acetyl fluoride according to the scheme:

$$Ti(OR)_4 + CH_3COF \rightarrow Ti(OR)_3F + CH_3COOR$$
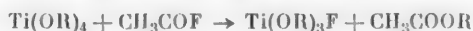
This reaction for the preparation of alkoxyfluoro-derivatives of other elements was studied earlier by A. Ia. Iakubovich, S. P. Makarov, and V. A. Ginsburg [2].

### EXPERIMENTAL

Preparation of diethoxyfluorostibine (I) from triethoxystibine and antimony trifluoride. Triethoxystibine was prepared according to the directions of Meerwein [3]. A mixture of 72.1 g of triethoxystibine (b. p. 101° at 17 mm, 76° at 4 mm) and 17.15 g of antimony trifluoride was heated, with stirring, at 140-150° with a reflux condenser for 7 hrs. As a result a homogeneous, crystalline mass with m. p. 60-70° was formed; the product was the double compound $Sb(OC_2H_5)_3 \cdot 3Sb(OC_2H_5)_2F$.

Found %: Sb 51.37; F 7.49. $C_{18}H_{45}O_9F_3Sb_4$. Calculated %: Sb 51.32; F 6.01.

On subsequent distillation of the substance in vacuo two fractions were obtained; the first had b. p. 72-77° at 2.5-3.5 mm, and its analysis corresponded to triethoxystibine.

Found %: Sb 47.24, 47.65. $C_6H_{15}O_3Sb$. Calculated %: Sb 47.42.

The second fraction had b. p. 164-166° (7 mm) and m. p. 49-52° after two-fold distillation and consisted of (I).

Found %: Sb 52.63, 53.28; F 7.44, 7.68; $OC_2H_5$ 39.11, 39.39. $C_4H_{10}O_2FSb$. Calculated %: Sb 52.76; F 8.24; $OC_2H_5$ 39.0.

The yield of (I), calculated on the basis of the triethoxystibine entering into the reaction, amounted to 77%. (I) was a very hygroscopic, colorless, crystalline substance, soluble in benzene, alcohol, or acetone (all anhydrous).

Preparation of diisopropoxyfluorostibine (II) from triisopropoxystibine and antimony trifluoride. A mixture of 19.7 g of $Sb(iso-OC_3H_7)_3$ [3] (b. p. 80-81° at 3.5 mm) and 4 g of $SbF_3$ was heated, with stirring, at 120-140° with a reflux condenser for 5 hrs. There was obtained a crystalline substance with m. p. about 40°, consisting of the double compound $Sb(iso-OC_3H_7)_3 \cdot 3Sb(iso-OC_3H_7)_2F$.

Found %: Sb 45.63. $C_{27}H_{63}O_9F_3Sb_4$. Calculated %: Sb 45.36.

When this compound was heated in vacuo, it decomposed, as a result of which triisopropoxystibine and (II) were formed. After distillation there was a certain amount of antimony trifluoride in the residue.

Both these esters distilled together at 68-72° (2-3 mm). Crystals of (II) could be obtained from the distillate on cooling.

Found %: Sb 46.17, 46.12; iso-$OC_3H_7$ 46.26; F 7.19. $C_6H_{14}O_2FSb$. Calculated %: Sb 47; iso-$OC_3H_7$ 45.66; F 7.34.

The yield of (II) was about 20%, calculated on the basis of the triisopropoxystibine entering into the reaction. (II) was a colorless, crystalline substance with m. p. 55°, very hygroscopic, readily soluble in alcohol or benzene (both anhydrous), and less soluble in acetone.

Preparation of triethoxytitanium fluoride (III). a) From ethyl orthotitanate and antimony trifluoride. Ethyl orthotitanate was prepared according to published directions [4]. A mixture of 15.75 g of $Ti(OC_2H_5)_4$ (b. p. 145° at 8.5 mm) and 4.118 g of $SbF_3$ was heated at 120-130° with stirring for 3 hrs. There was obtained a homogeneous, crystalline mass of the double compound $Sb(OC_2H_5)_3 \cdot 3Ti(OC_2H_5)_3F$, m. p. 82°.

Found %: Sb 15.08. $C_{24}H_{60}O_{12}SbF_3Ti_3$. Calculated %: Sb 14.12.

On subsequent distillation of this compound in vacuo, two fractions were obtained. The first fraction, having b. p. 62-64° (2 mm), consisted of triethoxystibine.

Found %: Sb 47.33. $C_6H_{15}O_3Sb$. Calculated %: Sb 47.42.

The yield, calculated on the basis of the double compound taken for distillation, was nearly quantitative.

The second fraction, which had b. p. 162-163° (2 mm) and m. p. 75-78°, was (III).

Found %: Ti 24.22, 23.15; $OC_2H_5$ 67.05; F 9.38. $C_6H_{15}O_3FTi$. Calculated %: Ti 23.73; $OC_2H_5$ 66.86; F 9.41.

The yield was 52.3%, calculated on the basis of the double compound taken for distillation. Triethoxytitanium fluoride (III) is a colorless, crystalline, very hygroscopic substance, readily soluble in benzene, ether (both absolute), alcohol, or acetone (both anhydrous); it dissolves better on heating.

b) From ethyl orthotitanate and acetyl fluoride. A mixture of 9.1 g of $Ti(OC_2H_5)_4$ and 2.5 g of $CH_3COF$ was heated about 8 hrs in a sealed tube in a boiling water bath.

When the tube was opened, no acetyl fluoride was found. On distillation two fractions were obtained; the first had b. p. 77° and amounted to 1.5 g (ethyl acetate), whereas the second had b. p. 162-164° (2 mm) after two-fold distillation and corresponded to (III). Yield 6.2 g (85.5%).

Preparation of triisopropoxytitanium fluoride (IV) from isopropyl orthotitanate and antimony trifluoride. A mixture of 12.54 g of isopropyl orthotitanate (b. p. 93° at 6 mm) [4] and 2.63 g of $SbF_3$ was heated at 120-140° with stirring for 6 hrs. As a result a white, crystalline substance having the composition $Sb(iso-OC_3H_7) \cdot 3Ti(iso-OC_3H_7)_3F$ was obtained.

Found %: Sb 11.91. $C_{36}H_{84}O_{12}F_3Sb$. Calculated %: Sb 11.82.

On distillation in vacuo of 74 g of this compound, two fractions were obtained; the first had b. p. 67-74° (2.5 mm) and corresponded to triisopropoxystibine, whereas the second, distilled at 140-150° (6 mm) and solidified to a crystalline substance with m. p. 83-85°. The yield of (IV) was 30%, calculated on the basis of the double compound taken for distillation.

Found %: Ti 19.91, 19.17. $C_9H_{21}O_3FTi$. Calculated %: Ti 19.64.

Triisopropoxytitanium fluoride (IV) is a colorless, crystalline, very hygroscopic substance, readily soluble in benzene or ethyl alcohol (both anhydrous); in anhydrous acetone it dissolves better on heating.

Preparation of tributoxytitanium fluoride (V). a) From butyl orthotitanate and antimony trifluoride. A mixture of 30 g of $Ti(OC_4H_9)_4$ (b. p. 164-166° at 1.5 mm) [4] and 5.26 g of $SbF_3$ was heated at 130-160° for 6 hrs with stirring. A homogeneous liquid was obtained. On distillation of the reaction mass (32.32 g) in vacuo, two fractions were obtained after several distillations; the first (5.74 g), which had b. p. 121-124° (2 mm), corresponded to $Sb(OC_4H_9)_3$.

Found %: Sb 35.77. $C_{12}H_{27}O_3Sb$. Calculated %: Sb 35.73.

The yield was 62.5%, calculated on the basis of the liquid taken for distillation.

The second fraction, which had b. p. 175-180° (2 mm) (m. p. 45-48°), corresponded to (V).

Found %: Ti 16.42; $OC_4H_9$ 76.8; F 7.04. $C_{12}H_{27}O_3FTi$. Calculated %: Ti 16.75; $OC_4H_9$ 76.6; F 6.65.

The yield was 30.0%, calculated on the basis of the liquid taken for distillation. The product was a colorless, crystalline, very hygroscopic substance, readily soluble in anhydrous benzene; in alcohol and acetone (both anhydrous) it dissolved better on mild heating.

b) From butyl orthotitanate and acetyl fluoride. A mixture of 17 g of $TiOC_4H_9)_4$ and 3.1 g of $CH_3COF$ was heated about 8 hrs in a sealed tube in a boiling water bath. A homogeneous liquid was obtained.

On distillation of the reaction liquid, two fractions were obtained; the first (5.2 g ), which had b. p. 123-124°, was butyl acetate, whereas the second, which had b. p. 199-200° (3.5 mm), corresponded to (V). Yield 9.8 g (68.9%).

## SUMMARY

1. It has been established that dialkoxyfluorostibines are obtained in the reaction of antimony trifluoride with trialkoxystibines.

2. Trialkoxytitanium fluorides and the corresponding trialkoxystibines have been isolated in the reaction of alkyl orthotitanates with antimony trifluoride.

3. It has been shown that this reaction proceeds through intermediate double compounds of the types $Sb(OR)_3 \cdot 3Sb(OR)_2F$ and $Sb(OR)_3 \cdot Ti(OR)_3F$, which decompose with the formation of dialkoxyfluorostibines and trialkoxytitanium fluorides.

4. It has been established that alkoxyfluoro-derivatives of titanium may be obtained also through the reaction of alkyl orthotitanates with acetyl fluoride.

Certain alkoxymonofluoro-derivatives of titanium and of trivalent antimony, which are not described in the literature, have been prepared.

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# INVESTIGATION OF A SERIES OF ORGANIC SULFUR COMPOUNDS

## IV. SYNTHESIS OF β-CHLOROETHANESULFONYL CHLORIDE

B. M. Gladshtein, I. P. Kuliulin, and L. Z. Soborovskii

β-Chloroethanesulfonyl chloride, as was shown earlier [1, 2], is an essential starting material in the synthesis of fluoroanhydrides of sulfonic acids of the ethane, ethylene, cyclopropane, pyrazoline, and pyrazole series. The reaction which was carried out — that of potassium fluoride with halogenated ethanesulfonyl chlorides and fluorides — made it possible to accomplish a direct transition from the stated compounds to sulfonyl fluorides of the olefin series, several more of which were synthesized in accordance with the scheme.
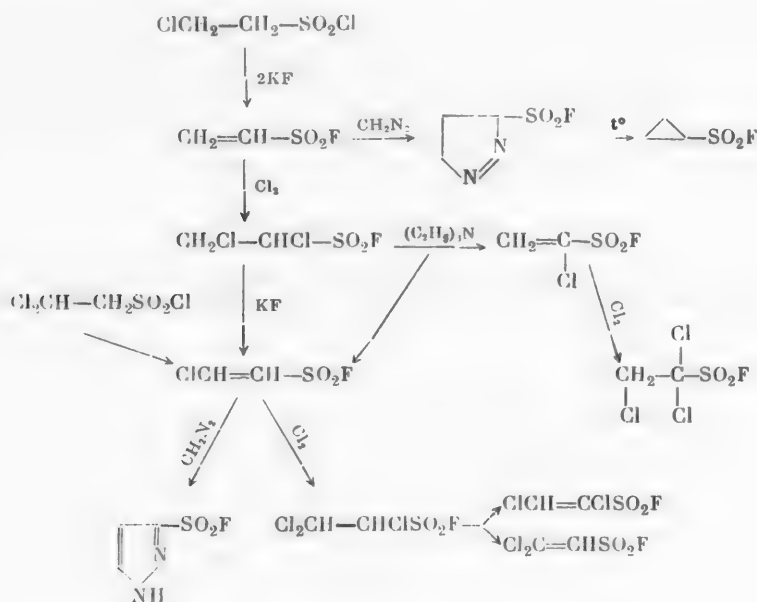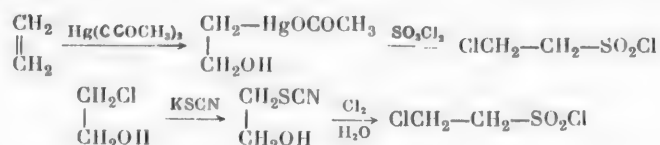


Thus the availability both of ethylenesulfonyl fluoride itself and of substances synthesized on the basis thereof is determined by the availability of the original β-chloroethanesulfonyl chloride.

The methods of synthesis of β-chloroethanesulfonyl chloride described in the literature are based on the action of phosphorus pentachloride on salts of isethionic acid, which, in turn, are obtained either by the addition of a bisulfite to ethylene oxide [3] or by the hydrolysis of carbyl sulfate [4]. Patents were issued [5] on the preparation of β-chloroethanesulfonyl chloride according to the scheme:

$$ClCH_2-CH_2Cl \xrightarrow{Na_2SO_2} ClCH_2-CH_2SO_2ONa \xrightarrow{PCl_5} ClCH_2-CH_2SO_2Cl$$

Kohler [6] showed that β-chloroethanesulfonyl chloride is formed also on heating ethane-1,2-disulfonyl chloride. Other authors obtained β-chloroethanesulfonyl chloride in 62.7% yield through the oxidative chlorination of β-chloroethyl thiocyanate, formed from 1,2-dichloroethane and ammonium thiocyanate in an ethanol medium [7]. Attempts to synthesize β-chloroethanesulfonyl chloride according to the schemes given below were unsuccessful.

$$
\begin{array}{c}
CH_2 \\
\parallel \\
CH_2
\end{array}
\xrightarrow{Hg(C\,COCH_3)_2}
\begin{array}{c}
CH_2-HgOCOCH_3 \\
\mid \\
CH_2OH
\end{array}
\xrightarrow{SO_2Cl_2}
ClCH_2-CH_2-SO_2Cl
$$

$$
\begin{array}{c}
CH_2Cl \\
\mid \\
CH_2OH
\end{array}
\xrightarrow{KSCN}
\begin{array}{c}
CH_2SCN \\
\mid \\
CH_2OH
\end{array}
\xrightarrow[H_2O]{Cl_2}
ClCH_2-CH_2-SO_2Cl
$$

Positive results were obtained by us in the study of the following processes:

$$
S\begin{cases}CH_2-CH_2OH \\ CH_2-CH_2OH\end{cases}
\xrightarrow[Cl_2,\ H_2O]{HCl,\ illumination}
$$

$$
S\begin{cases}CH_2-CH_2Cl \\ CH_2-CH_2Cl\end{cases}
\xrightarrow[illumination]{Cl_2,\ H_2O}
\quad \longrightarrow \quad ClCH_2-CH_2-SO_2Cl \ .
$$
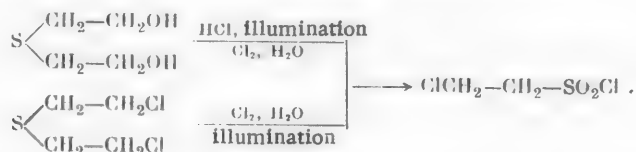
Experiment showed that the thiodiglycol, on chlorination in a concentrated hydrochloric acid medium, is converted to β-chloroethanesulfonyl chloride, with a yield greater than 50%. The importance of illumination, especially in the second half of the process, should be emphasized. Carrying this reaction out in the dark caused the yield of β-chloroethanesulfonyl chloride to fall to 5%.

In the oxidative chlorination of thiodiglycol there are formed together with β-chloroethanesulfonyl chloride, various chlorine-substituted hydrocarbons, of which pentachloroethane and symmetrical tetrachloroethane were isolated.

The described process of conversion of thiodiglycol to β-chloroethanesulfonyl chloride goes through an intermediate stage of formation of β,β'-dichlorodiethyl sulfide. The correctness of this is confirmed by the fact that β,β'-dichlorodiethyl sulfide itself, as we found, gives a satisfactory yield of β-chloroethanesulfonyl chloride when chlorinated in an aqueous medium with illumination.

Thus the reaction of oxidative chlorination of aliphatic [8] and cyclic sulfides [9], applied to thiodiglycol and β,β'-dichlorodiethyl sulfide, provides a convenient preparative method for the synthesis of β-chloroethane-sulfonyl chloride.

The development of this method made it possible to combine sulfides of the aliphatic series, thiodiglycol, and β,β'-dichlorodiethyl sulfide by direct transitions with β-chloroethanesulfonyl chloride, ethylenesulfonyl fluoride, and other substances synthesized on the basis of the last series of conversions described by us earlier [1, 2].

EXPERIMENTAL

Chlorination of thiodiglycol. 50 g of thiodiglycol was stirred with 360 ml of hydrochloric acid ( d 1.19) and a slow current of chlorine was passed into the mixture for 3 hrs at 65-70°. Then the mixture was cooled to 20° and illuminated by a lamp (400 w), and a vigorous current of chlorine was passed into the mixture. The reaction temperature was 50-55°. At the end of the reaction (which was indicated by the passage of chlorine through the mixture) the oil which separated out was drawn off, dried with calcium chloride, and distilled in vacuo. The following fractions were obtained: the first, having b. p. 33-92° (20 mm), and the second, having b. p. 92-102° (20 mm). On repeated distillation these fractions were isolated from the first:

B. p. 146-147° (759 mm), $n^{15}D$ 1.4928, $d_4^{25}$ 1.5942 and b. p. 160-162° (759 mm), $n^{20}D$ 1.5022, $d_4^{25}$ 1.6601.

Literature data for 1,1,2,2-tetrachloroethane: b. p. 146.2° [10], $n^{15}D$ 1.4967 [11], $d_4^{25}$ 1.5881 [12].

Literature data for pentachloroethane: b. p. 161.9° [10], $n^{15}D$ 1.5054 [11], $d_4^{25}$ 1.6712 [12].

Thus the first fraction contains pentachloroethane and symmetrical tetrachloroethane.

The isolation and identification of other chlorine-substituted ethanes having a lower degree of chlorination will be carried out in the future.

On distillation of the second fraction (35 g), $\beta$-chloroethanesulfonyl chloride was obtained (yield 52.5%).

B. p. 196-199° (751 mm), $n^{20}D$ 1.4918, $d_4^{20}$ 1.5487. Found: M 163.6, $MR_D$ 30.53. $C_2H_4O_2SCl_2$. Calculated: M 163.03, $MR_D$ 30.1.

Literature data for $\beta$-chloroethanesulfonyl chloride [13]: b. p. 68° (5 mm), $n^{20}D$ 1.4920, $d_4^{20}$ 1.555, $MR_D$ 30.72.

Chlorination of $\beta,\beta'$-dichlorodiethyl sulfide. Into a flask were put 177 g of $\beta,\beta'$-dichlorodiethyl sulfide [b. p. 117-118° (20 mm)] and 1 liter of water and, with vigorous stirring and illumination by a lamp (200 w), a current of chlorine was passed into the mixture at such a rate as to insure its complete absorption. The temperature of the mixture reached 40-50° within 1 hr and was maintained at that level throughout the reaction (at first the mixture had to be cooled with water). The end of the reaction was indicated by the appearance of a faint, yellowish-green tint in the mixture. The oil which separated out was drawn off, washed with water, dried with calcium chloride, and distilled in vacuo; the fraction with b. p. 93-106° (20 mm) was isolated.*

By repeated distillation at atmospheric pressure there was obtained a substance with b. p. 198-204° (735 mm), $n^{20}D$ 1.4898, $d_4^{20}$ 1.5434, $MR_D$ 30.63. Yield 51%.

## SUMMARY

The synthesis of $\beta$-chloroethanesulfonyl chloride by the oxidative chlorination of thiodiglycol (in a hydrochloric acid medium) or $\beta,\beta'$-dichlorodiethyl sulfide (in an aqueous medium) with illumination has been described.

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* Pentachloroethane and symmetrical tetrachloroethane were isolated also from the lower fraction, as described in the preceding experiment.

** Original Russian pagination. See C. B. translation.

# INVESTIGATION IN THE FIELD OF ALKANESULFONIC ACIDS

## XVIII. CHLORINATION OF ALKANESULFONIC ACID TOLUIDIDES

### A. G. Kostsova and N. T. Borisova

Alkanesulfonic acid toluidides are described in the literature as antipyretics and antineuralgics [1]; chlorinated toluidides are unknown.

The purpose of the present work was to study the chlorination of alkanesulfonic acid o- and p-toluidides, using ethane- and butanesulfotoluidides as examples.

The reaction was carried out under the conditions described by us for the anilides of the stated sulfonic acids [2]. The reaction temperature and time of chlorination were varied; the rate at which chlorine was passed in remained constant in all experiments.

As our experiments showed, the yields of chlorination products sharply decrease in the presence of ZnO; change of temperature from 0 to 40° has little effect, although somewhat better results are observed at reduced temperatures; increase in the amount of solvent decreases the yields of products. On chlorination of the p-toluidides, mainly chloro-p-toluidides are formed at first, together with a negligible quantity of tetrachloro-p-toluidides, of which only ethanesulfotetrachloro-p-toluidide was isolated in pure form and characterized; butanesulfotetrachloro-p-toluidide was isolated in the form of a heavy, viscous mass, which could not be crystallized and purified. On increase of the chlorination time the yields of chloro-p-toluidides decrease, whereas those of tetrachlorotoluidides increase somewhat.

On chlorination of o-toluidides there are formed only chloro-o-toluidides, the quantity of which sharply decreases as the chlorination time increases. Tetrachloro-o-toluidides were not isolated.

The position of the chlorine in chloro-p-toluidides was proved by their hydrolysis to 3-chloro-p-toluidine, which was identified through its acetyl derivative.

For this purpose the chloro-o-toluidides were hydrolyzed and the resulting chloro-o-toluidine was then acetylated, but the data obtained were not sufficiently conclusive, since N-acetyl-5-chloro-o-toluidine and N-acetyl-4-chloro-o-toluidine have very similar constants. However, one argument in favor of the presence of 5-chloro-o-toluidine is the fact that many reactions carried out by us with toluidines showed that the stronger orienting substituent in these compounds is the alkanesulfonamido group and not the methyl; this argument is supported by the chlorination of the p-toluidide.

Chloro-o-toluidides are colorless, crystalline compounds, whereas chloro-p-toluidides are usually isolated in the form of heavy yellow oils, which distill in vacuo without decomposition and crystallize on standing or on cooling. Both of these and the others dissolve in organic solvents, and also in dilute alkali, from which they are precipitated on acidification; they are insoluble in water. By treatment in ether solution with metallic sodium, the sodium salt of ethanesulfochloro-o-toluidide was obtained. The acetyl derivatives of ethane- and butanesulfochloro-o-toluidides were obtained by treatment with acetic anhydride.

Tetrachloro-p-toluidides differ sharply in their properties from chlorotoluidides, in that they are insoluble in the cold in alcohol, ether, or dilute alkali, do not form salts with metallic sodium, are not alkylated, and are not acylated. These properties of tetrachloro-p-toluidides, so unusual for N-arylamides, are obviously due to steric hindrances resulting from the presence of two chlorine atoms in the ortho-position with respect to the NH

TABLE 1

| Name of compound | Melting point | Content (in %) | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| | | N | | Cl | | S | |
| | | found | calc. | found | calc. | found | calc. |
| Ethanesulfo-3-chloro-p-toluidide $C_9H_{12}O_2NSCl$ | 44—46° | 5.92 | 5.99 | 15.22 | 15.20 | 13.63 | 13.70 |
| Ethanesulfotetrachloro-p-toluidide $C_9H_9O_2NSCl_4$ | 140—142 | 4.17 | 4.15 | 41.73 | 42.10 | 9.78 | 9.49 |
| Butanesulfo-3-chloro-p-toluidide $C_{11}H_{16}O_2NSCl$ | 38—40 | 5.10 | 5.35 | 13.46 | 13.54 | 12.08 | 12.22 |
| Ethanesulfo-5-chloro-o-toluidide $C_9H_{12}O_2NSCl$ | 92—94 | 6.09 | 6.00 | 15.70 | 15.20 | 13.30 | 13.70 |
| Butanesulfo-5-chloro-o-toluidide $C_{11}H_{16}O_2NSCl$ | 113—114 | 5.25 | 5.35 | 13.59 | 13.54 | 12.12 | 12.22 |
| Sodium salt of ethanesulfo-5-chloro-o-toluidide $C_9H_{11}O_2NSClNa$ | -- | 5.40 | 5.47 | — | — | — | — |
| Ethanesulfo-N-acetyl-5-chloro-o-toluidide $C_{11}H_{14}O_3NSCl$ | 108—109 | 5.40 | 5.14 | — | — | — | — |
| Butanesulfo-N-acetyl-5-chloro-o-toluidide $C_{13}H_{18}O_3NSCl$ | 71 | 4.33 | 4.81 | — | — | — | — |

group. A list of the compounds obtained, their constants, and analytical data are given in Table 1.

## EXPERIMENTAL

Chlorination of ethane- and butanesulfonic acid p-toluidides. Into a solution of the p-toluidide in $CCl_4$ was passed a stream of chlorine gas, dried with sulfuric acid, at a rate of 3 ml/sec. At the end of the chlorination the reaction mixture was left until the next day; the $CCl_4$ was then distilled off or evaporated, and from the remaining viscous, yellow oil the reaction products — chlorotoluidides and tetrachlorotoluidides — were isolated by two methods.

1. The oil was treated with 5% alkali. During this treatment the tetrachlorotoluidide did not dissolve, but, in the case of ethanesulfo-p-toluidide, separated out in the form of a finely crystalline precipitate and in the case of butanesulfo-p-toluidide, precipitated in the form of a grayish, viscous mass; chloro-p-toluidides dissolved in the alkali, which in this case became quite dark. Since chlorination by-products apparently dissolved in the alkali along with the chlorotoluidide, only a very insignificant quantity of the chlorotoluidide could be isolated from the alkaline solution on acidification.

2. On treatment of the oil with alcohol the tetrachlorotoluidide, which is insoluble in cold alcohol, precipitated, whereas the chlorotoluidide passed into alcoholic solution, the alcohol was driven off in a water bath, and the residual chlorotoluidide distilled in vacuo at 180-190° (5 mm) for the ethane- and at 185-195° (4 mm) for the butanesulfo-derivative in the form of a viscous light-yellow oil, which crystallized on cooling. The chloro-p-toluidides were recrystallized from aqueous alcohol, and ethanesulfotetrachloro-p-toluidide, from hot alcohol; the tetrachloro-p-toluidide of butanesulfonic acid could not be purified and crystallized. We chlorinated butane-sulfonic acid p-toluidide also in other solvents, for instance, ether, benzine, nitrobenzene, and glacial acetic acid, but were not able to obtain the crystalline tetrachlorotoluidide. The results of certain experiments in the chlorination of ethane- and butanesulfonic acid p-toluidides are given in Table 2.

Chlorination of ethane- and butanesulfonic acid o-toluidides. The chlorination was carried out as in the preceding case. In this case the crystalline chloro-o-toluidide precipitated within 5-8 min; it was filtered out, but after its removal the filtrate still contained a yellow oil, from which the crystalline tetrachloro-o-toluidide could not be isolated. The results of certain experiments in the chlorination of ethane- and butanesulfonic acid o-toluidides are given in Table 3.

The sodium salt of ethanesulfonic acid chloro-o-toluidide was prepared by the method described by us earlier [3]. From 2 g of the chloro-o-toluidide 1.4 g (67.3%) of the salt was obtained. The latter was a very

TABLE 2

| Initial quantity of o-toluidide (in g) | Quantity of CCl$_4$ (in ml) | Time of passage of Cl$_2$ (in min) | Reaction temperature | Reaction products isolated (in %) | |
|---|---|---|---|---|---|
| | | | | chloro-toluidide | tetrachloro-toluidide |
| Ethanesulfo-p-toluidide | | | | | |
| 5 | 40 | 90 | 0—3° | 25.6 | 37.2 |
| 5 (+ ZnO) | 40 | 90 | 0—3 | — | 3.0 |
| 2.5 | 15 | 45 | 30—8 | 34.1 | 17.3 |
| 2.5 | 15 | 15 | 15—10 | 78.5 | Traces |
| Butanesulfo-p-toluidide | | | | | |
| 6 | 25 | 90 | 2—7 | 21.7 | ... |
| 6 | 25 | 120 | 2—7 | 14.5 | ... |
| 6 | 25 | 20 | 0—3 | 64.4 | ... |

TABLE 3

| Initial quantity of o-toluidide (in g) | Quantity of CCl$_4$ (in ml) | Time of passage of Cl$_2$ (in min) | Temperature | Chloro-o-toluidide isolated (in %) |
|---|---|---|---|---|
| Ethanesulfo-o-toluidide | | | | |
| 9 | 40 | 15 | 2—8° | 66.5 |
| 5 (+ ZnO) | 25 | 8 | 2—8 | 48.5 |
| 4.5 | 25 | 14 | 30—18 | 53.1 |
| Butanesulfo-o-toluidide | | | | |
| 5 | 20 | 15 | 20—0 | 75.0 |
| 5 | 20 | 30 | 20—0 | 59.7 |
| 5 | 20 | 15 | 40—15 | 67.0 |
| 5 | 20 | 30 | 38—16 | 56.8 |
| 5 (+ ZnO) | 20 | 15 | 18—2 | 16.7 |

hygroscopic, amorphous, white powder. On acetylation of ethane- and butanesulfonic acid chloro-o-toluidides by the method described earlier [2], 1.24 g (69%) of the acetyl derivative was obtained from 1.6 g of ethanesulfo-chloro-o-toluidide and 3.4 g of acetic anhydride, and 0.9 g (66.6%) of the acetyl derivative was obtained from 1.2 g of butanesulfochloro-o-toluidide and 3.2 g of acetic anhydride. The acetyl derivatives were recrystallized from aqueous alcohol.

Hydrolysis of chlorotoluidides. The hydrolysis was carried out with sulfuric acid (1 : 1) for several hours until addition of water to a test sample ceased to cause precipitation. 1 g of the substance and 10 ml of acid were taken. At the end of the reaction the mixture was alkalized, the separated chlorotoluidine was extracted with ether, and the ether extract was dried with potash; then the ether was distilled off and the residual oil (chloro-toluidine) was treated with acetyl chloride. The resulting precipitate, after evaporation of excess acetyl chloride, was recrystallized from aqueous alcohol. On hydrolysis of ethane- and butanesulfonic acid chloro-p-toluidides and subsequent acetylation there was obtained N-acetyl-3-chloro-p-toluidine, m. p. 114-117°; according to literature data, m. p. 118° [4]. On hydrolysis of ethane- and butanesulfonic acid chloro-o-toluidides there was obtained N-acetyl-5-chloro-o-toluidine, m. p. 138-139°; according to literature data, m. p. 140° [4]. Analysis of the acetyl derivatives of the chlorotoluidines for nitrogen gave satisfactory results.

## SUMMARY

1. The chlorination of ethane- and butanesulfonic acid o- and p-toluidides under various conditions has been studied.

2. Ethane- and butanesulfonic acid chloro-o- and p-toluidides, as well as ethanesulfonic acid tetrachloro-p-toluidide, have been isolated and characterized.

3. The sodium salt of ethanesulfonic acid chloro-o-toluidide and the N-acetyl derivatives of ethane- and butanesulfonic acid chloro-o-toluidides have been prepared and characterized.

4. The structure of chloro-p-toluidides has been proved by the reaction of hydrolysis.

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# ALKYLATION OVER AN ALUMINOSILICATE CATALYST ACTIVATED BY GASEOUS HYDROGEN CHLORIDE

## I. ALKYLATION OF BENZENE BY ALKYL CHLORIDES

### I. F. Radzevenchuk

In 1943 it was observed that gumbrin in the presence of hydrogen chloride can catalyze the alkylation reaction at 70° [1]. At that time this reaction seemed improbable and was not investigated in detail. During the last few years reactions over aluminosilicates have come into wide use. The reactions of polymerization and depolymerization [2], catalytic cracking [3], and alkylation [4] have been studied. Therefore, we have attempted to carry out reactions between benzene and alkyl halides under the conditions characteristic of reactions with $AlCl_3$.

In the presence of a natural aluminosilicate (gumbrin), dried at 160-170° to constant weight, and gaseous hydrogen chloride at 70-76°, the alkylation of benzene by isopropyl chloride, n-butyl chloride, and isobutyl chloride was carried out. As the result of a series of experiments alkylbenzenes were obtained in the following yields: propylbenzenes, 70%, and butylbenzenes, 50 and 70%, respectively (yields calculated on the basis of alkyl halide).

As preliminary experiments showed, an essential point for insuring the success of the alkylation at 70-76° is the drying of the gumbrin at 160° and its treatment with hydrogen chloride in a medium consisting of the alkylating reagents. The gumbrin had to be dried until the interstitial water was removed. For this it was heated to constant weight in a thermostat at 160-170°; in this case it lost 14.2% water. Drying at 310-320 and 425-450° gave only an insignificant increase in the percentage of water removed (0.4%), and the activity of the catalyst was not increased. At 500° the gumbrin lost 23.5% water and its activity diminished. It may be assumed that at this temperature partial decomposition of the structural hydroxyls takes place with formation of the "anhydrous modification" of montmorillonite [5]. The structure of the silicate and hydrargillite layers changes, and therefore the activity of the gumbrin falls. It is generally known that montmorillonites can absorb liquids. Thus, when ethylene glycol was absorbed by montmorillonite, the glycol molecules formed double layers among the blocks of the montmorillonite lattice [6, 7]. It is possible that after removal of the interstitial water the mixture of benzene and alkyl chloride took its place; thus the reagents closely approached the active centers of the aluminosilicate and formed complexes with it, and a catalytic reaction became more probable. However, as was stated earlier, thermal treatment of the gumbrin is not in itself sufficient to make the alkylation reaction go at 70°. A second, no less important condition is the passage of a current of dry hydrogen chloride through the benzene-alkyl halide mixture. The alkylation reaction did not take place with gumbrin dried at 160°, but passage of a current of dry hydrogen chloride through a suspension of the clay in the reagents for 15 min was enough to make the reaction begin. Propylbenzenes were formed in 40% yield. Increase in the time of passage of HCl to 3 hrs decreased the yield of alkylbenzenes. As was ascertained by a series of experiments, it is expedient to pass the HCl through for 1-1.5 hr. In the literature [8, 9] there is a statement that treatment of $Al_2O_3$ by gaseous hydrogen chloride at 300-400° substantially heightens its catalytic properties in isomerization reactions. The authors explain the increase in the activity of the $Al_2O_3$ by the presence on its surface of bound chloride ions resulting from the reaction of surface hydroxyl groups with HCl. The increase in the activity of dry gumbrin on treatment with gaseous HCl in the alkylation experiments also can be explained by taking into account the structure of montmorillonite clays and the presence of Si, isomorphically substituted for Al [10]. The yield of alkylbenzenes was affected also by the fact that the clay and hydrogen chloride gas were added not to benzene, but to a benzene-alkyl halide mixture. It is possible that, as was proved for $AlCl_3$ [11], the catalysis here is ionic in character.

The activity acquired by the clay is retained for some time. After the alkylation reaction was carried out, the clay layer had catalytic properties. New portions of alkyl halide and benzene were successfully alkylated with it.

The process of alkylation is accompanied by isomerization of the alkyl halides taken into the reaction. For instance, in the alkylation of isobutyl chloride, di-tert-butylbenzene was obtained. Such isomerization also accompanies the reaction with $AlCl_3$, as is generally known, and is observed also in vapor-phase alkylation over an aluminosilicate catalyst [4]. The molar ratio of alkyl halide to benzene in all experiments was equal to $0.2:1$. In the reaction with $AlCl_3$ [12] such a ratio was stated to be most expedient for obtaining monoalkyl derivatives.

## EXPERIMENTAL

A three-neck flask with stirrer was charged with 30-60 g of gumbrin dried at 160-170°. One-third of the benzene and alkyl halide, taken into the reaction, was added. The alkyl halides were prepared from the corresponding alcohols by treatment with conc. HCl in the presence of $ZnCl_2$ [13]. Both the benzene and the alkyl halides were carefully dried over $CaCl_2$ and distilled before the reaction. Their constants corresponded to literature data. The benzene-alkyl halide mixture was heated in a water bath to 60-70°; a bent tube reaching to the bottom was inserted in the second neck of the flask, and a strong current of dry HCl was passed through the tube. The third neck of the flask was coupled to a bulb condenser. The end of the condenser was closed by a calcium-chloride drying tube. During the first 7 min the HCl was absorbed by the clay, and after that it passed out through the drying tube.

Mechanical stirring was not used in this step. After 1-1.5 hrs the HCl current was stopped, the HCl delivery tube was taken out, and a dropping funnel was put in its place. The temperature of the bath was raised to 70°. The mechanical stirrer was turned on, and the rest of the benzene-alkyl halide mixture was added dropwise through the dropping funnel during 1-1.5 hr. The progress of the reaction was marked by the evolution of HCl. After addition of the mixture the temperature was raised to 76-78°. Heating and stirring were continued for 3-8 hrs, until the evolution of HCl ceased. After settling, the upper hydrocarbon layer was decanted from the blackened clay, washed with 10% NaOH and dried over $CaCl_2$. The clay was transferred to a flask, and the adsorbed hydrocarbons were removed by steam distillation. The hydrocarbons obtained were dried and distilled. In all cases one distillation through a column was sufficient for the isolation of pure alkylbenzenes. Therefore we obtained purer individual alkylation products than with $AlCl_3$ prepared according to published data [14].

Alkylation of benzene by isopropyl chloride. The experiments were conducted with a molar ratio of benzene to isopropyl chloride, equal to $1:0.22$. The effects on the yield of alkylbenzenes of the temperature at which the clay was dried, the time of passage of hydrogen chloride, the order and time of addition of the reagents, and the temperature and duration of the reaction were investigated. Better results were obtained in the case where the clay was dried at 160-170° (loss of water, 14.2%). Time of passage of hydrogen chloride, 1 hr (at 60°). Time of addition of the rest of the benzene-isopropyl chloride mixture, 75 min. Temperature 70-76°. Reaction time 7 hrs. Yield of propylbenzenes, 70% (these were 87% isopropylbenzene). After the first distillation through a column the isopropylbenzene (first fraction) had the following constants:

B. p. 151-152.5°, $n_D^{20}$ 1.14915, $d_4^{20}$ 0.8615, $MR_D$ 40.40; calc. 40.20. M 120, 123; calc. 120.2.

The second fraction, obtained in the quantity 6%, distilled at 190-192° and had $n_D^{20}$ 1.4918; it obviously consisted of diisopropylbenzene with a slight admixture of isopropylbenzene. The residue had $n_D^{20}$ 1.4960.

Alkylation of benzene by isobutyl chloride. The isobutyl chloride had b. p. 68-70°. The ratio of benzene to isobutyl chloride was equal to $1:0.20$. 25 g of clay per 100 g of benzene was taken. The remaining conditions were the same as in the preceding experiment. The yield of alkylation products amounted to 70% (based on the isobutyl chloride taken). After distillation through a column two fractions were isolated. The residue (18%) was also distilled through a column. The first fraction (10%) had b. p. 166-169° and $n_D^{20}$ 1.4908. Obviously this was tert-butylbenzene (b. p. 169°, $n_D^{20}$ 1.4908 [15]). The second fraction (42%) had the constants:

B. p. 169-170°, $n_D^{20}$ 1.4920, $d_4^{20}$ 0.8656, $MR_D$ 44.9; calc. 44.8. M 135.4; calc. 134.1. Literature data for isobutylbenzene: b. p. 170°, $n_D^{20}$ 1.4928, $d_4^{20}$ 0.8673 [15].

On distillation a fraction with b. p. 190° was isolated from the residue in the quantity 7%. Crystals separated out from this and from the residue on cooling. After several recrystallizations from alcohol they had m. p. 78°. Among the butylbenzenes the only solid substance is di-tert-butylbenzene, m. p. 77.8° [15].

The formation of di-tert-butylbenzene indicates that the original alkyl halide was isomerized.

Alkylation of benzene by n-butyl chloride. Alkylation under the conditions of the preceding experiments gave only 50% alkylbenzenes. This low yield is possibly due to the lesser activity of butyl chloride. By distillation through a column a fraction (38%) with b. p. 168-171°, $n^{18}$D 1.4900, and a residue (12%) were isolated. Melting point of the diacetylamino derivative, 192°. M 131; calc. 134.1. Obviously this fraction consisted of sec-butylbenzene. The residue had $n^{20}$D 1.4940 and M 146 and was probably a mixture of polybutylbenzenes.

## SUMMARY

The alkylation of benzene by isopropyl chloride, isobutyl chloride, and butyl chloride has been carried out in the presence of gumbrin, dried at 160°, and gaseous hydrogen chloride. Reaction temperature 70-76°. It has been established that the principal reaction products are monoalkylbenzenes.

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# DEPENDENCE OF THE YIELD AND THE QUALITY OF BENZENESULFONYL CHLORIDE ON THE EXCESS OF CHLOROSULFONIC ACID AND ADDITION OF SODIUM SALTS

L. I. Levina, S. N. Patrakova, and D. A. Patrushev

A number of authors [1-4] have been concerned with the problem of raising the yield and improving the quality of commercial sulfonyl chlorides.

No indications are to be found in the literature concerning the effect of additions of salts of alkali metals on the quality of the sulfonyl chlorides produced. In the present study we investigated the effect of the excess of chlorosulfonic acid and of additions of salts of sodium on the yield and the quality of benzenesulfonyl chloride.

As shown by B. Iu. Iasnitskii [5] and A. A. Spryskov [6, 7], the reaction of formation of benzenesulfonyl chloride is a reversible one and, consequently, the yield of benzenesulfonyl chloride should be raised by increased excess of chlorosulfonic acid, which fact is confirmed by experimental data (see Table). At the same time, the quality of benzenesulfonyl chloride (the content of sulfones as admixtures to it) to an insignificant degree does depend on the excess of chlorosulfonic acid.

Dependence of Yield and Quality of Benzenesulfonyl Chloride on the Ratio of Benzene and Chlorosulfonic Acid and Additions of Sodium Salts

| Molar ratio of benzene to chlorosulfonic acid | Yield of commercial benzenesulfonyl chloride (%) | | | Analysis of benzenesulfonyl chloride (in %) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | acidity | | | content of sulfones | | | content of benzenesulfonyl chloride | | |
| | no addition of salts | addition of Na$_2$SO$_4$ | addition of NaCl | no addition of salts | addition of Na$_2$SO$_4$ | addition of NaCl | no addition of salts | addition of Na$_2$SO$_4$ | addition of NaCl | no addition of salts | addition of Na$_2$SO$_4$ | addition of NaCl |
| 1 : 2.5 | 78.2 | — | — | 0.11 | — | — | 4.9 | — | — | 94.8 | — | — |
| 1 : 3.0 | 83.1 | — | — | 0.17 | — | — | 4.6 | — | — | 95.2 | — | — |
| 1 : 5.0 | 87.8 | — | — | 0.80 | — | — | 4.0 | — | — | 95.0 | — | — |
| 1 : 2.5 | — | 64.2 | — | — | 0.09 | — | — | 1.68 | — | — | 98.0 | — |
| 1 : 3.0 | — | 78.6 | — | — | 0.05 | — | — | 1.03 | — | — | 98.0 | — |
| 1 : 5.0 | — | 80.0 | — | — | 0.50 | — | — | 0.20 | — | — | 99.3 | — |
| 1 : 2.5 | — | — | 71.8 | — | — | 0.25 | — | — | 3.10 | — | — | 96.3 |
| 1 : 3.0 | — | — | 82.0 | — | — | 0.10 | — | — | 2.07 | — | — | 97.8 |
| 1 : 5.0 | — | — | 86.9 | — | — | 0.43 | — | — | 1.80 | — | — | 97.1 |

It follows from the above table that the addition of sodium sulfate leads to a decline of the yield of benzenesulfonyl chloride with a small excess of chlorosulfonic acid (0.5 mole over the stoichiometric ratio). With excess of chlorosulfonic acid equal to 1 mole or more, the addition of sodium sulfate does not affect the yield but does raise the quality of benzenesulfonyl chloride by lowering the content of sulfones from 4.0-4.9 to 0.2-1.68%. A similar effect on the process of chlorosulfonation is exerted by the addition of sodium chloride to the original chlorosulfonic acid. The lowering of the amount of sulfone admixture may be explained by the formation of sodium benzenesulfonate, which is an inhibitor of the formation of sulfones in sulfonation of benzene by a high percentage oleum [8].

## EXPERIMENTAL*

The experiments were run in a round-bottomed flask provided with a reflux condenser, a stirrer, a dropping funnel, a thermometer and a tube for leading off the hydrogen chloride. To twice-distilled chlorosulfonic acid (containing dried sodium chloride or sulfate) there was added from the dropping funnel over 6 hrs the required amount of benzene. The reaction was run at 20-26°. The content of the principal substance and of sulfones was determined in the resulting benzenesulfonyl chloride by saponification with N solution of sodium hydroxide. The acidity of the product was determined by means of 0.1 N solution of sodium hydroxide.

## SUMMARY

The yield of benzenesulfonyl chloride is raised from 78.2% to 87.8% by increase of the amount of chlorosulfonic acid from 2.5 to 5 moles per 1 mole of benzene. The lowering of the sulfone content is achieved by the addition of sodium sulfate or chloride to the original chlorosulfonic acid.

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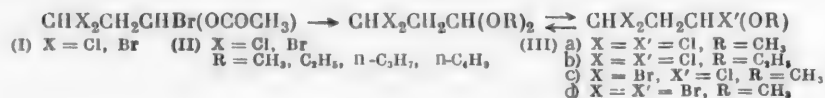
* With participation of K. K. Turanova.
** Original Russian pagination. See C. B. translation.

# ACETALS OF β,β-DIHALO SUBSTITUTED PROPIONALDEHYDES

T. V. Protopopova and A. P. Skoldinov

In our previous communication [1] there was described the application of derivatives of β,β-dihalo substituted propionaldehydes with the general formula $CHX_2CH_2CHBr(OCOCH_3)$ (I, X = Cl or Br) for the synthesis of various heterocyclic compounds. The acetals of these aldehydes were also of interest since they could serve as starting materials for the preparation of the thus far unknown free β,β-dihalo substituted propionaldehydes and β-halo substituted acroleins. Only dimethyl acetal of β,β-dichloropropionaldehyde [2] had been described among such acetals up to the present time.

$$CHX_2CH_2CHBr(OCOCH_3) \longrightarrow CHX_2CH_2CH(OR)_2 \rightleftharpoons CHX_2CH_2CHX'(OR)$$

(I) X = Cl, Br    (II) X = Cl, Br    (III) a) X = X' = Cl, R = CH_3
                R = CH_3, C_2H_5, n-C_3H_7, n-C_4H_9    b) X = X' = Cl, R = C_2H_5
                                        c) X = Br, X' = Cl, R = CH_3
                                        d) X = X' = Br, R = CH_3

By the action of an appropriate alcohol on (I) we prepared in satisfactory yields a series of acetals (II) which were colorless liquids, which possessed characteristic odors and were distillable in vacuum without decomposition; they were stable to storage in the cold. These acetals were relatively stable in respect to dilute acids; however, treatment with acids under more drastic conditions led to cleavage of hydrogen halides and formation of polymeric products. The results of action of basic reagents on acetals (II) will be disclosed in a future communication.

Acetals (II) are transformed into the corresponding 1,1,3-trihalo-3-alkoxypropanes (III)* by cleavage of an alkyl chloride in the reaction with phosphorus pentachloride or thionyl chloride in an inert solvent or without a solvent. One of the halogen atoms in these compounds is quite mobile — it is readily hydrolyzed even in the cold by water, which fact permits one to titrate quantitatively the compounds of type (III) by mercurometric methods. Such properties of compounds (III) agree completely with their structure of alkyl $\alpha,\gamma,\gamma$-trihalopropyl ethers.

The preparation of (IIId) could not be accomplished by the reaction of substance (II, X = Br) with phosphorus pentabromide owing to the brominating action of the latter; (IIId) was prepared by treatment of (IIIc) with hydrogen bromide [3]. As the result of reaction of (III) with alcohols one obtains compounds (II) again, which fact was demonstrated in the example of transformation of (IIIa) and (IIIb) into the corresponding acetals.

(II) and (III), just like other functional derivatives of malonodialdehyde, are capable of condensation with nitrogenous compounds analogous to condensations previously described for (I). For example, in the reaction of such compounds with hydrazine, there is formed pyrazole, with hydroxylamine there is formed isoxazole [1], with urea there is formed 2-hydroxypyrimidine, with thiourea there is obtained 2-mercaptopyrimidine [4], with guanidine there is formed 2-aminopyrimidine [2, 4, 5], etc. There is no need to cite these reactions in the experimental section, but one should note that the reactivity of the presently described compounds declines in the series (III) > (I) > (II), which fact is connected with the relative ease of liberation of the aldehyde group in compounds of this type.

## EXPERIMENTAL

### Preparation of the Acetals

A mixture of 0.1 mole of 1,1-dihalo-3-bromo-3-acetoxypropane and 1.5-2.0 moles of the corresponding alcohol, after standing for four days at room temperature, were poured into a cooled solution of sodium bicarbonate

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* The transformation of (II) into (III) proceeds especially smoothly under the action of thionyl chloride in the presence of catalytic amounts of tertiary amines.

and the separated oil was extracted with ether; the residue after the removal of ether was fractionated in vacuo. In this manner there were prepared the following acetals:

Dimethyl acetal of β,β-dichloropropionaldehyde (yield 70%):

B. p. 67-68° (18.5 mm), $n^{20}D$ 1.4400, $d_4^{20}$ 1.1954, $MR_D$ 38.09; calc. 38.30.

Literature data [2]: b. p. 70° (18 mm).

Diethyl acetal of β,β-dichloropropionaldehyde (yield 80%).

B. p. 65-66° (6 mm), $n^{20}D$ 1.4380, $d_4^{20}$ 1.1118, $MR_D$ 47.50; calc. 47.55. Found %: C 41.67, 41.48; H 6.85, 6.91; Cl 35.08, 34.96. $C_7H_{14}O_2Cl_2$. Calculated %: C 41.79; H 6.96; Cl 35.32.

Di-n-propyl acetal of β,β-dichloropropionaldehyde (yield 55%).

B. p. 77-78° (2-2.5 mm), $n^{20}D$ 1.4428, $d_4^{20}$ 1.0725, $MR_D$ 56.59; calc. 56.76. Found %: C 47.35, 47.24; H 7.38, 7.87. $C_9H_{18}O_2Cl_2$. Calculated %: C 47.16; H 7.86.

Di-n-butyl acetal of β,β-dichloropropionaldehyde (yield 75%).

B. p. 108-109° (3 mm), $n^{20}D$ 1.4460, $d_4^{20}$ 1.0358, $MR_D$ 66.18; calc. 66.02. Found %: C 51.66, 51.35; H 8.63, 8.50. $C_{11}H_{22}O_2Cl_2$. Calculated %: C 51.36; H 8.56.

Dimethyl acetal of β,β-dibromopropionaldehyde (yield 82%).

B. p. 59-60° (2 mm), $n^{20}D$ 1.4912, $d_4^{20}$ 1.7194, $MR_D$ 44.17; calc. 44.10. Found %: C 22.54, 22.67; H 4.02, 4.00; Br 66.25, 61.46. $C_5H_{10}O_2Br_2$. Calculated %: C 22.90; H 3.81; Br 61.00.

Diethyl acetal of β,β-dibromopropionaldehyde (yield 62%).

B. p. 70-71° (1.5 mm), $n^{20}D$ 1.4755, $d_4^{20}$ 1.5211, $MR_D$ 53.63; calc. 53.34. Found %: C 29.28, 29.25; H 5.02, 5.03; Br 54.85, 54.68. $C_7H_{14}O_2Br_2$. Calculated %: C 28.95; H 4.82; Br 55.17.

Di-n-propyl acetal of β,β-dibromopropionaldehyde (yield 60%).

B. p. 97-98° (1.5 mm), $n^{20}D$ 1.4740, $d_4^{20}$ 1.4228, $MR_D$ 62.77; calc. 62.58. Found %: C 33.97, 33.26; H 5.70, 5.76; Br 50.17, 50.07. $C_9H_{18}O_2Br_2$. Calculated %: C 33.96; H 5.66; Br 50.31.

Di-n-butyl acetal of β,β-dibromopropionaldehyde (yield 50%).

B. p. 120-121° (2 mm), $n^{20}D$ 1.4728, $d_4^{20}$ 1.3469, $MR_D$ 71.87; calc. 71.81. Found %: C 38.32, 38.33; H 6.38, 6.29; Br 46.15, 46.01. $C_{11}H_{22}O_2Br_2$. Calculated %: C 38.15; H 6.35; Br 46.24.

## Preparation of α,γ,γ-Trihalopropyl Alkyl Ethers

1,1,3-Trichloro-3-methoxypropane. To a mixture of 18.1 g (0.104 mole) of dimethyl acetal of β,β-dichloropropionaldehyde and 12.5 g (0.105 mole) of distilled thionyl chloride, preheated to 65°, there was added one drop of pyridine; after the evolution of sulfur dioxide became weaker, the mixture was heated until the gas evolution ceased completely by raising the bath temperature gradually to 90-95°. After fractionation in vacuum, with protection from atmospheric moisture, there was obtained 13.8 g (78%) of the product.

B. p. 45.5-48° (7 mm), $n^{20}D$ 1.4630, $d_4^{20}$ 1.3201, $MR_D$ 37.07; calc. 36.92. Found %: Cl⁻ 20.03, 20.01; $Cl_{total}$ 60.36, 60.24. $C_4H_7OCl_3$. Calculated %: Cl⁻ 20.00; $Cl_{total}$ 60.00.

1,1,3-Trichloro-3-ethoxypropane. To a suspension of 9.1 g (0.043 mole) of phosphorus pentachloride in 15 ml of dry carbon tetrachloride there was rapidly added 8.6 g (0.042 mole) of diethyl acetal of β,β-dichloropropionaldehyde. After completion of the exothermic reaction, the mixture was refluxed for 20 min longer and was then fractionated in vacuum; there was obtained 7.3 g (91%) of a fraction with b. p. 49-53° (4 mm). The substance was distilled twice.

B. p. 38.5-40° (1.5 mm), $n^{20}D$ 1.4578, $d_4^{20}$ 1.2543, $MR_D$ 41.67; calc. 41.53. Found %: C 31.73, 31.70; H 4.77, 4.80; Cl⁻ 18.22, 18.47. $C_5H_9OCl_3$. Calculated %: C 31.41; H 4.71; Cl⁻ 18.53.

<u>1,1-Dibromo-3-chloro-3-methoxypropane</u> was prepared analogously (yield 90%).

B.p. 53.5-55° (1.5 mm), $n^{20}D$ 1.5165. Found %: $Cl^-$ 13.21, 13.18. $CHBr_2CH_2CHCl(OCH_3)$. Calculated %: $Cl^-$ 13.32.

<u>1,1,3-Tribromo-3-methoxypropane.</u> 1,1-Dibromo-3-chloro-3-methoxypropane (15.7 g; 0.059 mole) was saturated with dry hydrogen bromide; the excess of hydrogen bromide was removed by blowing with dry air and the residue was fractionated in vacuum. There was obtained 9.4 g (50%) of a liquid which fumed strongly in air.

B. p. 83-85° (2 mm), $n^{20}D$ 1.5495, $d_4^{20}$ 2.1231, $MR_D$ 46.33; calc. 45.61. Found %: $Br^-$ 25.39, 25.10; $Br_{total}$ 76.67, 76.73. $CHBr_2CH_2CHBrOCH_3$. Calculated %: $Br^-$ 25.72; $Br_{total}$ 77.17.

<u>Reaction of 1,1,3-trichloro-3-ethoxypropane with alcohol.</u> A mixture of 4 g of 1,1,3-trichloro-3-ethoxy-propane and 17 ml of anhydrous ethyl alcohol was kept for 20 hrs at room temperature, after which it was poured into a solution of sodium bicarbonate and the separated oil was extracted with ether. After vacuum fractionation there was obtained 3.8 g (90%) of diethyl acetal of $\beta,\beta$-dichloropropionaldehyde; b. p. 64-66° (6 mm), $n^{20}D$ 1.4355.

Dimethyl acetal of $\beta,\beta$-dichloropionaldehyde was prepared analogously (74%); b. p. 66-66.5° (18.5 mm), $n^{23}D$ 1.4360.

## SUMMARY

1. A series of acetals with general formula $CHX_2CH_2CH(OR)_2$, where X = Cl or Br, R = $CH_3$, $C_2H_5$, $n-C_3H_7$ or $n-C_4H_9$, was prepared and some of the properties of these compounds were studied.

2. Alkyl $\alpha,\gamma,\gamma$-trihaloalkyl ethers with the general formula $CHX_2CH_2CHX'(OR)$ were prepared by the reaction of the acetals with phosphorus pentachloride or thionyl chloride.

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* Original Russian pagination. See C. B. translation.

# HETEROCYCLIC COMPOUNDS

## LXII. STEREOCHEMISTRY OF 1-ACYL-2,5-DIMETHYL-4-PIPERIDONES

I. N. Nazarov, N. S. Prostakov, and N. N. Mikheeva

Recently the 2,5-dimethyl-4-piperidones [2] preparable by the reaction of propenyl isopropenyl ketone [2] with ammonia or primary amines, have been used widely in our laboratory for the synthesis of various 4-piperidols and their esters. Among the latter are the propionates of stereoisomeric 1,2,5-trimethyl-4-phenyl-4-piperidols — Promedol, Isopromedol and $\alpha$-Promedol — prepared in our laboratory [3]. Promedol ($\gamma$-isomer) turned out to be a highly active analgesic which exceeded morphine in activity by about 2-3-fold. Isopromedol ($\beta$-isomer) turned out to be more active than Promedol by 2-fold. However, the most active pain-relieving properties were possessed by $\alpha$-Promedol, which exceeded the activity of Isopromedol by a factor of 2. The dependence of physiological activity on the spatial structure was also established for the propionates of stereoisomeric 1,3-dimethyl-4-phenyl-4-piperidols ($\alpha$-Prodin and $\beta$-Prodin [4]).
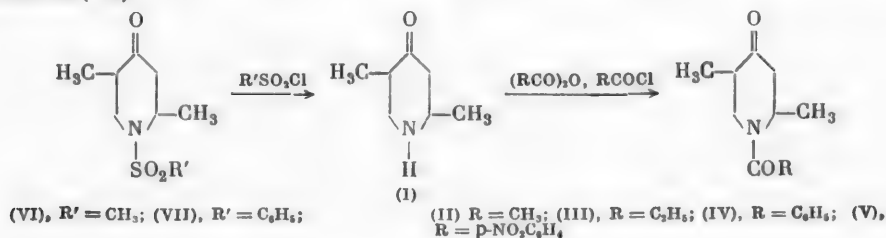
We supposed that during the study of stereochemistry of 4-piperidones we might obtain data which would permit us to approach the establishment of the steric or spatial structure of 4-phenyl-4-piperidols and their esters.

2,5-Dimethyl-4-piperidone (I) can exist in two stereoisomeric forms (cis and trans). Up to the present time these stereoisomeric forms had not been isolated which fact is evidently connected with the ease of their mutual transformations.



(I) cis form      (I) trans form
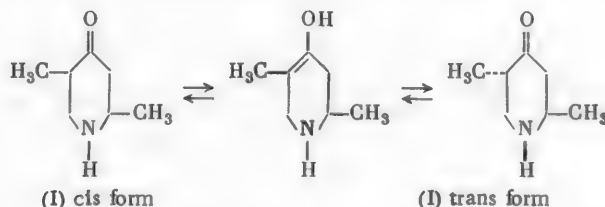
One may expect that in the series of 1-acyl-2,5-dimethyl-4-piperidones having an amide nitrogen with considerably reduced basic properties, the mutual transformations of the isomeric piperidones would not proceed with such facility and therefore it would be possible to isolate and to study the individual stereoisomers.

For this reason we prepared during the treatment of 2,5-dimethyl-4-piperidone (I) with acid anhydrides and acyl chlorides, as well as sulfonyl chlorides, the following 1-acyl-2,5-dimethyl-4-piperidones: 1-acetyl (II) [5], 1-propionyl (III), 1-benzoyl (IV) [5], 1-p-nitrobenzoyl (V), 1-methylsulfonyl (VI) and 1-benzenesulfo-2,5-dimethyl-4-piperidones (VII).



(VI), $R' = CH_3$; (VII), $R' = C_6H_5$;      (I)      (II) $R = CH_3$; (III), $R = C_2H_5$; (IV), $R = C_6H_5$; (V), $R = p\text{-}NO_2C_6H_4$

The diamide (VIII) was prepared in low yield by acylation of piperidone (I) with the chloride of adipic acid.
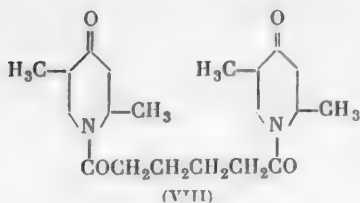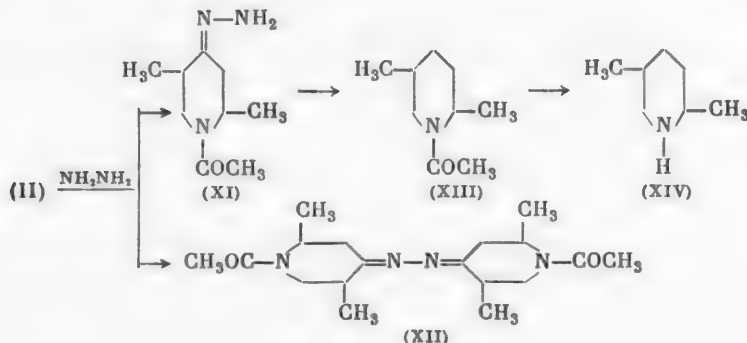
1-Acetyl-2,5-dimethyl-4-piperidone (II) was isolated in a crystalline (IIa) and a liquid state (IIb) in 1 : 1 ratio. The proportion of the crystalline and the liquid fractions depends on the method of treatment. By subjecting the liquid fraction to repeated distillation and by simply heating it to 150-160° it was possible to change this fraction totally into the crystalline isomer.

The crystalline and the liquid isomers form two different oximes (IXa) and (IXb), which after reduction with sodium in alcohol yielded two different 1-acetyl-2,5-dimethyl-4-aminopiperidines (Xa) and (Xb).

(VIII)

(IIa) and (IIb)     (IXa) and (IXb)     (Xa) and (Xb)
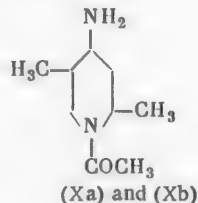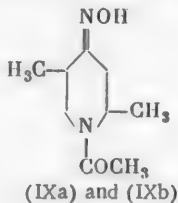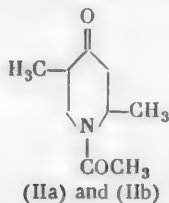
1-Benzoyl-2,5-dimethyl-4-piperidone (IV) was also isolated in fractions of crystalline and liquid form. Piperidones (II) and (IV) were hydrolyzed by 20% aqueous solution of sulfuric acid to the original 2,5-dimethyl-4-piperidone (I). An attempt to prepare hydrazones of both isomeric 1-acetyl-2,5-dimethyl-4-piperidones (IIa) and (IIb) failed to give the desired positive results. Both from the crystalline isomer (IIa) and from the liquid fraction containing mainly isomer (IIb) there was formed one and the same hydrazone (XI) which corresponded to the more stable stereoisomeric form of 1-acetyl-2,5-dimethyl-4-piperidone (IIa). The less stable form of piperidone (IIb) evidently isomerizes during the preparation of the hydrazone into the more stable form (IIa) under the influence of the alkaline medium. The preparation of hydrazone of 1-acetyl-2,5-dimethyl-4-piperidone is accompanied by the formation of a considerable amount of the azine (XII).

The hydrazone of 1-acetyl-2,5-dimethyl-4-piperidone (XI) was further reduced by the Kizhner method to 1-acetyl-2,5-dimethylpiperidine (XIII), which was deacetylated to 2,5-dimethylpiperidine (XIV).

(II) $\xrightarrow{NH_2NH_2}$

(XI)     (XIII)     (XIV)

(XII)

1-p-Nitrobenzoyl- and 1-methylsulfonyl-2,5-dimethyl-4-piperidones (V) and (VI) were prepared in the form of mixtures of crystalline isomers.

Piperidone (VI) was isolated in two crystalline stereoisomeric forms (VIa) and (VIb) by fractional crystallization. As in the case of the above-described 1-acetyl-2,5-dimethyl-4-piperidone (II), the lower melting isomer of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIb) is the less stable one and transforms itself into the higher melting isomer (VIa) on being heated to 120° or on being heated with aluminum oxide in chloroform, the transformation being quantitative.

By acylation of 2,5-dimethyl-4-piperidone (I) with chloroacetyl chloride and subsequent treatment of the resulting 1-chloroacetyl-2,5-dimethyl-4-piperidone with diethylamine, as well as piperidine, there were prepared 1-diethylaminoacetyl- (XV) and 1-N-piperidylacetyl-2,5-dimethyl-4-piperidone (XVI).



(XV)          (XVI)
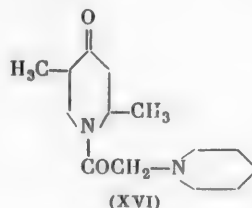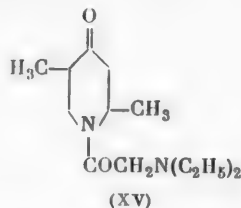
The hydrochloride of piperidone (XVI) produces a comparatively weak anesthetic action in 0.5% solution.

## EXPERIMENTAL

2,5-Dimethyl-4-piperidone (I). For preparation of (I) we used the mixture of 2-methyl-1,4-hexadien-3-one, 2-methyl-5-methoxy-1-hexen-3-one and 2-methyl-1,5-dimethoxy-3-hexanone (b. p. 71° at 16 mm, 62° at 4.5 mm), which was heated with aqueous ammonia solution, or with ammonium acetate at the boiling point of methanol if the reaction was run in a methanol solution, or at 90-95° if methanol was not employed. In the latter case, the reaction mixture was stirred energetically. The reaction of cyclization with the aqueous ammonia solution was run in a hermetically closed vessel; in other cases it was run in the usual round-bottomed flask with a reflux condenser or in a three-necked flask provided with a stirrer and a reflux condenser. Methanol was distilled off after the completion of heating, slight vacuum being used for the distillation, and then the mixture was treated, with cooling, with 18% hydrochloric acid until it became acid to Congo red. The unreacted ketones were extracted with ether. The residual aqueous solution was evaporated and treated with potassium hydroxide with cooling, until the amine layer formed. The amines were extracted 5-8 times with ether. The ethereal extracts were dried with calcined sodium sulfate or potassium carbonate after which the reaction products were distilled twice in vacuo. The 2,5-dimethyl-4-piperidone, after the two distillations, had b. p. 76-78° (9 mm), 66° (6 mm), $n^{20}$D 1.4676.

2,5-Dimethyl-4-piperidone acetate, formed in the reaction of cyclization by means of ammonium acetate, formed long colorless needle-like crystals with m. p. 92-94°.

Found %: N 7.46, 7.48. $C_9H_{17}O_3N$. Calculated %: N 7.49.

In the following table there are shown the yields of 2,5-dimethyl-4-piperidone after running the cyclization reaction: 1) with aqueous ammonia solution with an 8% excess of the latter; 2) with ammonium acetate (30% excess) in aqueous methanol; 3) under analogous conditions but without methyl alcohol.
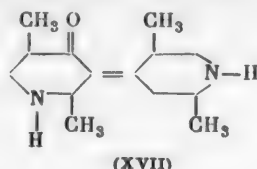
Yields of 2,5-Dimethyl-4-piperidone

| | Mixtures of ketones (g) | Ammonia (in g) | Acetic acid (g) | Water (in ml) | Methyl alcohol (in ml) | Duration of heating (in hrs) | Am't of 2,5-di-methyl-4-piperi-done ob-tained (g) | Recovery of ketones (g) | 2,5-Dimethyl-4-piperidone yield based on ketone mixture (in %) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | ketones used for reaction | reacted ketones (conversion) |
| 1 | 310 | 36 | — | 115 | 150 | 6 | 70 | 59.4 | 28 | 34.7 |
| 2 | 500 | 70 | 248 | 385 | 500 | 7 | 167.5 | 69.3 | 41.6 | 48.1 |
| 3 | 500 | 70 | 248 | 710 | — | 12 | 157 | 28 | 39.1 | 41.4 |

Note. The average molecular weight of the mixture of the starting ketones was taken to be 158.

Under all the conditions described above for the preparation of 2,5-dimethyl-4-piperidone there was formed a considerable amount of products with high boiling points along with a tarry residue. From the fractions boiling considerably above the piperidone there was isolated the product of its condensation — 2,5-dimethyl-3-(2',5'-

dimethyl-4'-piperidylidene)-4-piperidone (XVII), in the form of a viscous green liquid with b. p. 130-134° (2.5 mm), $n^{20}$D 1.4990. Its hydrochloride melted at 225° (from alcohol).



(XVII)

Found %: C 70.76, 71.31; H 9.58, 10.28; N 11.82, 11.50. $C_{14}H_{24}ON_2$. Calculated %: C 71.19; H 10.17; N 11.86.

1-Acetyl-2,5-dimethyl-4-piperidone (II). To 123.5 g of freshly distilled 2,5-dimethyl-4-piperidone there was added, with cooling and stirring, 146 g of acetic anhydride. The mixture was then heated for 8 hrs at 70-80°. It turned dark and became viscous. After the distillation of the acetic anhydride residue, the remaining material was twice distilled in vacuo. There was obtained 144.5 g of substance (II) with b. p. 134-136° (3 mm), $n^{20}$D 1.4900.

Found %: N 7.98, 8.21, 7.96, 8.03. $C_9H_{15}O_2N$. Calculated %: N 8.28.

The distilled piperidone crystallized in part. There was obtained 74 g of colorless crystals with m. p. 60-61°, which corresponded to piperidone (IIa).

Found %: N 8.10, 8.50. $C_9H_{15}O_2N$. Calculated %: N 8.28.

After the separation of the crystalline piperidone (IIa) there remained 70 g of the liquid isomer of the piperidone (IIb). 2 g of it was heated for 45 min at 150-160°. The mixture crystallized immediately after being cooled. There was isolated 0.7 g of piperidone (IIa) with m. p. 60-61°.

Hydrolysis of 1-acetyl-2,5-dimethyl-4-piperidone. 1-Acetyl-2,5-dimethyl-4-piperidone (IIa; 4.3 g) with m. p. 60-61° and 20 g of 20% sulfuric acid were refluxed for 5 hrs. The reaction mixture was carefully treated with sodium hydroxide. The upper layer of organic bases was taken up in ether and dried. After vacuum distillation there was obtained 2.7 g of 2,5-dimethyl-4-piperidone (I) with b. p. 71.5° (8.5 mm), $n^{21}$D 1.4670.

Oxime of 1-acetyl-2,5-dimethyl-4-piperidone (IXa) and (IXb). a) To a solution of 6 g of 1-acetyl-2,5-dimethyl-4-piperidone (IIa) with m. p. 60-61° and 3 g of hydroxylamine hydrochloride in 10 ml of water there was added 6 g of sodium bicarbonate. The resulting precipitate (6.5 g) of the oxime of 1-acetyl-2,5-dimethyl-4-piperidone (IXa) melted at 159-160°, after recrystallization from alcohol.

Found %: N 15.02, 15.32. $C_9H_{16}O_2N_2$. Calculated %: N 15.22.

b) Analogously, from 2 g of 1-acetyl-2,5-dimethyl-4-piperidone (IIb), 2 g of sodium bicarbonate, 1 g of hydroxylamine hydrochloride and 10 ml of water, the oxime (IXb) (1.2 g) with m. p. 179-181° (from alcohol)was prepared.

Found %: N 15.18, 15.36. $C_9H_{16}O_2N_2$. Calculated %: N 15.22.

1-Acetyl-2,5-dimethyl-4-aminopiperidine (Xa) and (Xb). a) To a boiling solution of 4 g of oxime (IXa) (m. p. 159-160°) in 50 ml of anhydrous alcohol there was added, in small pieces but quite rapidly, 5 g of metallic sodium. The last portion of sodium was dissolved by heating. The excess alcohol was distilled in slight vacuum and the residue was dissolved in water and repeatedly extracted with ether. After distillation of ether from the ethereal extract which had been dried with sodium sulfate, there remained 2 g of a liquid which was distilled in vacuum. There were obtained the following fractions: 1st, b. p. 45-53° (3 mm), 0.3 g, $n^{20}$D 1.4791; and 2nd, b. p. 138-140° (3 mm), 0.6 g, $n^{20}$D 1.4950.

From the second fraction there was obtained 0.5 g of hydrochloride of 1-acetyl-2,5-dimethyl-4-amino-piperidine (Xa) with m. p. 273-275° (from anhydrous alcohol).

Found %: N 13.36, 13.05. $C_9H_{19}ON_2Cl$. Calculated %: N 13.56.

b) The reduction of oxime of 1-acetyl-2,5-dimethyl-4-piperidone (IX b) (m. p. 179-181°) was run analogously; 1 g of the oxime, 1.3 g of sodium and 20 ml of anhydrous alcohol being used. Hydrogen chloride was passed into the ethereal solution of the base, after separation from the drying agent. An oil formed, which crystallized after addition of alcohol. After recrystallization from alcohol there was obtained 0.2 g of the hydrochloride of 1-acetyl-2,5-dimethyl-4-aminopiperidine (X b) with m. p. 328-331°.

Found %: N 13.87. $C_9H_{19}ON_2Cl$. Calculated %: N 13.56.

Hydrazone of 1-acetyl-2,5-dimethyl-4-piperidone (XI). To 40 g of 1-acetyl-2,5-dimethyl-4-piperidone (IIa) (m. p. 60-61°) there was added carefully with shaking and cooling 35 ml of 85% hydrazine hydrate. The mixture was heated on a boiling water bath for 30 min. The excess hydrazine hydrate was distilled off and the residue was twice distilled in vacuo. There was obtained 32 g of the hydrazone of 1-acetyl-2,5-dimethyl-4-piperidone (XI) with b. p. 162-164° (3 mm), $n^{20}D$ 1.5338.

Found %: N 22.48, 22.70. $C_9H_{17}ON_3$. Calculated %: N 22.95.

After distillation of hydrazone (XI) there remained a residue from which there was isolated the azine of 1-acetyl-2,5-dimethyl-4-piperidone (XII) with b. p. 225-230° (3 mm).

Found %: N 17.04, 16.80. $C_{18}H_{30}O_2N_4$. Calculated %: N 16.77.

1-Acetyl-2,5-dimethylpiperidine (XIII) and 2,5-dimethylpiperidine (XIV). 30 g of freshly distilled hydrazone of 1-acetyl-2,5-dimethyl-4-piperidone (XI) and 7 g of fused potassium hydroxide were heated in a flask, provided with a distilling condenser, up to 120°. Immediately a decomposition of the hydrazone began accompanied by a violent evolution of nitrogen and distillation of a liquid. The vapor temperature reached 130-200°. Additional 23 g of fused potassium hydroxide was added in small portions during the course of the decomposition. The distilled substance was dissolved in absolute ether, dried with potassium carbonate and distilled. There were obtained the following fractions: 1st, b. p. 137-138° (4.7 g), $n^{20}D$ 1.4440, and 2nd, b. p. 88-91° (3 mm) 5.9 g, $n^{20}D$ 1.4742.

The first fraction was a volatile liquid with a sharp amine odor, which was 2,5-dimethylpiperidine (XIV). Its hydrochloride, after two recrystallizations from acetone, melted at 196-197°.

Found %: Cl 23.74, 23.67. $C_7H_{16}NCl$. Calculated %: Cl 23.74.

The second fraction — a liquid with unpleasant odor — was 1-acetyl-2,5-dimethylpiperidine (XIII).

Found %: N 8.70, 9.04. $C_9H_{17}ON$. Calculated %: N 9.03.

2 g of 1-acetyl-2,5-dimethylpiperidine (XIII) was heated with 5 g of potassium hydroxide at about 200°. There distilled 1 g of a liquid, which yielded the above-described hydrochloride of 2,5-dimethylpiperidine by the conventional treatment.

1-Propionyl-2,5-dimethyl-4-piperidone (III). To a solution of 60 g of freshly distilled 2,5-dimethyl-4-piperidone in 100 ml of anhydrous benzene there was added, with cooling and stirring, 22 g of propionyl chloride dissolved in 50 ml of benzene. The reaction mixture was stirred for 2 hrs at room temperature. The resulting precipitate of the hydrochloride of the original piperidone was filtered off and washed with benzene. From the mother liquor there was isolated by a vacuum distillation 36.5 g of 1-propionyl-2,5-dimethyl-4-piperidone (III) with b. p. 123-126° (2.5 mm).

Found %: N 7.69, 7.79. $C_{10}H_{17}O_2N$. Calculated %: N 7.65.

From the resulting mixture of stereoisomeric 1-propionyl-2,5-dimethyl-4-piperidones (III) there was isolated the oxime with m. p. 103-104.5° (from aqueous alcohol).

Found %: N 14.07, 13.91. $C_{10}H_{18}O_2N_2$. Calculated %: N 14.14.

1-Benzoyl-2,5-dimethyl-4-piperidone (IV). To 150 g of freshly distilled 2,5-dimethyl-4-piperidone in 150 ml of benzene there was added with cooling and stirring a solution of 83 g of benzoyl chloride in 50 ml of benzene. The mixture was heated for 5 hrs at gentle reflux of benzene. The precipitate was filtered off and repeatedly washed on the filter with benzene and ether. There was obtained 65.4 g of the hydrochloride of 2,5-dimethyl-4-piperidone which was recrystallized from a mixture of acetone and alcohol. Thereby there was ob-

tained at first 45.6 g of crystals with m. p. 143-145°, while from the mother liquors there were obtained in succession three precipitates of 6.5, 5.8 and 0.7 g, whose melting points depended on the temperature at which the samples were introduced into the melting point apparatus. If the sample were heated gradually from 20-30°, it melted just as the first isolated portion of the crystals at 143-145°; if the sample were introduced into the apparatus preheated to 120-130°, the sample melted instantly.

The solvent was distilled from the mother liquor remaining after the isolation of the hydrochloride of 2,5-dimethyl-4-piperidone. The residue, 170.5 g, was a viscous red liquid which was treated with heating by means of three portions of ether of 300 ml each. During the distillation of the substance extracted with ether, the distillation being made in vacuum, there was obtained 117.5 g of 1-benzoyl-2,5-dimethyl-4-piperidone (IV) in the form of a viscous liquid with b. p. 173° (3 mm), $n_D^{20}$ 1.5480.

Found %: N 6.10, 6.10. $C_{14}H_{17}O_2N$. Calculated %: N 6.06.

The piperidone crystallized after addition of absolute ether and cooling.

The precipitate was filtered off and washed with ether. There was obtained 36 g of crystals with m. p. 60-67°, while from the mother liquor there was isolated further some 22.4 g of crystals with m. p. 58-63°. The first precipitate (36 g) was recrystallized from ether. There was obtained 27.3 g of one of the stereoisomeric forms of 1-benzoyl-2,5-dimethyl-4-piperidone with m. p. 65.5-67.5°.

Found %: N 6.53, 6.33. $C_{14}H_{17}O_2N$. Calculated %: N 6.06.

The oxime of this isomer melted at 172-173° (from alcohol).

After the isolation of crystalline fractions of the piperidone there remained an uncrystallizable oil substance which was a mixture of stereoisomeric 1-benzoyl-2,5-dimethyl-4-piperidones. From 3.8 g of this substance there was obtained 2.9 g of a mixture of oximes of stereoisomeric piperidones with m. p. 147-159° (from alcohol; one of the precipitates).

Found %: N 11.71, 11.39. $C_{14}H_{18}O_2N_2$. Calculated %: N 11.38.

In benzoylation of 2,5-dimethyl-4-piperidones under other conditions there were obtained the following results:

a) From 45 g of 2,5-dimethyl-4-piperidone and 42 ml of benzoyl chloride after heating to 90-95° for 4 hrs there was obtained 34 g of 1-benzoyl-2,5-dimethyl-4-piperidone and 12 g of the starting piperidone (I).

b) There was used 45 g of 2,5-dimethyl-4-piperidone, 60 g of sodium hydroxide dissolved in 105 ml of water and 84 g of benzoyl chloride. The reaction was run with cooling with ice water. There was obtained 53 g of 1-benzoyl-2,5-dimethyl-4-piperidone.

Hydrolysis of 1-benzoyl-2,5-dimethyl-4-piperidone. 2 g of 1-benzoyl-2,5-dimethyl-4-piperidone was heated for 10 hrs at 100° with 20 ml of 20% sulfuric acid. Benzoic acid was extracted with ether. From the aqueous solution, after an alkaline treatment and extraction with ether, there was isolated 1 g of a liquid, after the distillation of which in vacuo there was obtained 0.3 g of 2,5-dimethyl-4-piperidone (I) with b. p. 80°(9 mm), $n_D^{20}$ 1.4665. Picrate (from alcohol), m. p. 167-168°.

1-p-Nitrobenzoyl-2,5-dimethyl-4-piperidone (V). 56 g of 2,5-dimethyl-4-piperidone, 41.2 g of p-nitrobenzoyl chloride (m. p. 73-74.5°) and 200 ml of anhydrous benzene were heated for 5 hrs at the boiling point of benzene. The hydrochloride of 2,5-dimethyl-4-piperidone was filtered off and washed with 100 ml of benzene. The precipitate which remained after the distillation of benzene was recrystallized from acetone. There was obtained 22 g of a mixture of stereoisomeric 1-p-nitrobenzoyl-2,5-dimethyl-4-piperidones with m. p. 128-138°. By repeated crystallization from acetone there was isolated one of the stereoisomeric 1-p-nitrobenzoyl-2,5-dimethyl-4-piperidones (V) with m. p. 144-146°.

Found %: N 10.20, 10.39. $C_{14}H_{16}O_4N_2$. Calculated %: N 10.14.

1-Methylsulfonyl-2,5-dimethyl-4-piperidone (VI). Methanesulfonyl chloride (18.2 g) dissolved in 25 ml of anhydrous benzene was added slowly with cooling and stirring to a solution of 32.5 g of 2,5-dimethyl-4-piperidone (I) in 100 ml of benzene. After stirring for 2 hrs at room temperature the precipitate of the hydrochloride of 2,5-dimethyl-4-piperidone (21.5 g) was filtered off and washed repeatedly with benzene. The solvent was

distilled from the mother liquor under slight vacuum. There was obtained 35.2 g of a viscous light red oil. 2 g of this residue was subjected to a vacuum distillation. There was obtained 1.8 g of a substance with b. p. 130-136° (10 mm), which crystallized immediately in the receiver. After recrystallization from a mixture of acetone and ether there was isolated one of the stereoisomers of 1-methylsulfonyl-2,5-dimethyl-4-piperidones (VIa) with m. p. 98-100°.

Found %: N 7.15, 7.22. $C_8H_{15}O_3NS$. Calculated %: N 6.83.

To the remaining 33.2 g there was added 100 ml of absolute ether. The resulting precipitate was filtered off and washed with absolute ether. There was obtained 17.9 g of colorless crystals with m. p. 49-60°. From the mother liquor there were isolated two more precipitates of 4.4 g with 60-64° and 2.4 g with m. p. 58-65°. These were mixtures of stereoisomeric 1-methylsulfonyl-2,5-dimethyl-4-piperidones.

Analysis of precipitate with m. p. 49-60°.

Found %: N 6.68, 6.67. $C_8H_{15}O_3NS$. Calculated %: N 6.83.

The oxime obtained from the mixture of stereoisomeric 1-methylsulfonyl-2,5-dimethyl-4-piperidones melted at 151-155° (from alcohol).

Found %: N 13.15, 13.00. $C_8H_{16}O_3N_2S$. Calculated %: N 12.77.

1 g of the mixture of stereoisomeric piperidones (VI) with m. p. 49-60° was recrystallized twice from absolute ether. There was obtained 0.3 g of a second stereoisomeric form of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIb) with m. p. 76-78°, which melted at 58-63° in a mixed melting point with the above-described isomer (VIa) with m. p. 98-100°.

Found %: N 6.90, 6.99. $C_8H_{15}O_3NS$. Calculated %: N 6.83.

The oxime of the lower melting isomer of 1-methylsulfonyl-2,5-dimethyl-4-piperidone melted at 168.5-170° (from aqueous acetone). The oxime of the high melting isomer of 1-methylsulfonyl-2,5-dimethyl-4-piperidone had m. p. 166-167° (from aqueous acetone). The mixed melting point of the two oximes of isomeric piperidone (VI) was 148-157°.

Isomerization of low melting isomer of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIb) into the high-melting isomer (VIa). a) 1-Methylsulfonyl-2,5-dimethyl-4-piperidone (VIb; 0.1 g; m. p. 76-78°) was heated without a solvent for 1.5 hr at 100-120°. After addition of absolute ether there was isolated 0.07 g of crystals with m. p. 93-95°, which did not give a depression in mixed melting point with the high melting isomer of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIa).

b) A solution of 0.2 g of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIb) with m. p. 76-78° in 20 ml of dry chloroform was heated on a water bath with stirring for 2 hrs with 3 g of aluminum oxide. After distillation of chloroform and addition of ether, the residue crystallized. There was isolated 0.15 g of the high melting isomer of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIa) with m. p. 96-98°.

c) 1.5 g of a mixture of stereoisomeric 1-methylsulfonyl-2,5-dimethyl-4-piperidones (VI) with m. p. 49-60° was heated without a solvent for 20 min at 120-130°. After addition of 2 ml of acetone there formed a precipitate which, after being washed with ether, was heated in acetone solution with activated carbon. There was obtained 0.52 g of crystals with m. p. 95-97°, which in mixed melting point with the above-described sample of 1-methylsulfonyl-2,5-dimethyl-4-piperidone (VIa) gave no depression.

1-Benzenesulfonyl-2,5-dimethyl-4-piperidone (VII). 2,5-Dimethyl-4-piperidone (17 g), 40 ml of a 12% aqueous solution of sodium hydroxide and 42 g of benzenesulfonyl chloride were heated for 8 hrs on a water bath with energetic stirring. A crystalline precipitate (25 g) formed on cooling; this was 1-benzenesulfonyl-2,5-dimethyl-4-piperidone with m. p. 124-126° (from anhydrous alcohol).

Found %: N 5.06, 5.10. $C_{13}H_{17}O_3NS$. Calculated %: N 5.24.

1,1'-Adipoylbis (2,5-dimethyl-4-piperidone)(VIII). 20 g of 2,5-dimethyl-4-piperidone and 7.6 g of the chloride of adipic acid, dissolved in 40 ml of benzene, were heated for 2.5 hrs at the boiling point of benzene. After distillation of benzene, the residue was dissolved in 20 ml of water, treated with sodium hydroxide and then

with 200 ml of ether. After drying of the ethereal solution with sodium sulfate and distillation of the ether, there was obtained 23.4 g of an oily substance from which there was vacuum distilled 9 g of the initial 2,5-dimethyl-4-piperidone (I). The remaining viscous mass was treated, with heating, with 4 portions of ether, 30 ml each. From the combined ethereal extracts there formed, after cooling and partial removal of ether, a colorless precipitate (0.9 g) of 1,1'-adipoylbis(2,5-dimethyl-4-piperidone) with m.p. 104-108° (after washing with absolute ether).

Found %: N 7.46, 7.76. $C_{20}H_{32}O_4N_2$. Calculated %: N 7.69.

1-Diethylaminoacetyl-2,5-dimethyl-4-piperidone (XV). To a solution of 17 g of 2,5-dimethyl-4-piperidone in 2.5 ml of benzene there was added with cooling and stirring a solution of 22 ml of chloroacetyl chloride in 25 ml of benzene. The red homogeneous solution was heated for 5 hrs at the boiling point of benzene. Then, 30 ml of diethylamine was added and heating was continued for 4 hrs at the boiling point of the amine. The benzene and the excess diethylamine were distilled off in vacuo. The residue was dissolved in water and was treated with sodium carbonate until saturated. The reaction products were extracted with ether and were vacuum distilled after having been dried. There was obtained 14 g of 1-diethylaminoacetyl-2,5-dimethyl-4-piperidone, in the form of a viscous liquid with b. p. 145° (3 mm).

Found %: N 11.63, 11.56. $C_{13}H_{24}O_2N_2$. Calculated %: N 11.66.

There was also obtained 7.4 g of a substance boiling at 60-145° (3 mm) and a residue of 5.5 g which dissolved readily in hydrochloric acid.

1-N-Piperidylacetyl-2,5-dimethyl-4-piperidone (XVI). 2,5-Dimethyl-4-piperidone (22.7 g ), 17 ml of chloroacetyl chloride and 50 ml of benzene were heated for 2 hrs at the boiling point of benzene. The excess chloroacetyl chloride and benzene were distilled off in vacuo. To the residue there was added 50 ml of benzene and 40 ml of freshly distilled piperidine. The mixture was heated for 4 hrs at 50-60°. The piperidine and benzene were distilled off in vacuo and the residue was dissolved in water and treated with sodium carbonate, after which an ether extraction was made.

After distillation of the reaction products in vacuum there was obtained 17.5 g of 1-N-piperdylacetyl-2,5-dimethyl-4-piperidone (XVI) in the form of a sirupy liquid with b. p. 136° (2.5 mm).

Found %: N 10.84, 10.78. $C_{14}H_{24}O_2N_2$. Calculated %: N 11.11.

1-N-Piperidylacetyl-2,5-dimethyl-4-piperidone hydrochloride melted at 205-207° after recrystallization from acetone.

Found %: N 9.81, 9.81. $C_{14}H_{25}O_2N_2Cl$. Calculated %: N 9.70.

## SUMMARY

A series of 1-acyl-2,5-dimethyl-4-piperidones was prepared. Some of these were obtained in two geometrically isomeric forms (cis and trans). It was shown that one of the isomeric piperidones had less stability and isomerized relatively readily into the more stable form.

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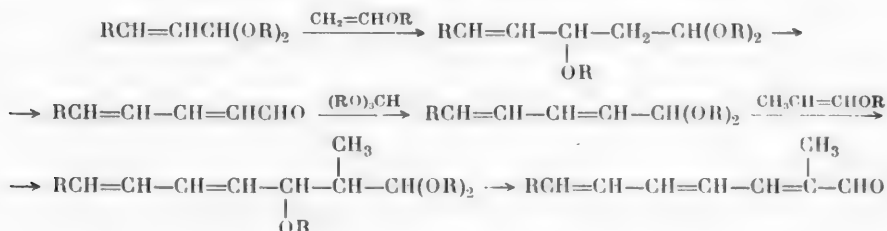* Original Russian pagination. See C. B. translation.

# CONDENSATION OF ACETALS WITH 1-ETHOXYDIENES

## A NEW METHOD OF SYNTHESIS OF POLYENE ALDEHYDES OF ISOPRENE TYPE

### I. N. Nazarov    and Zh. A. Krasnaia

Vinyl ethers have been successfully used in recent years for the synthesis of polyene aldehydes of the carotenoid series.

In the condensation of acetals with vinyl ethyl or propenyl ethyl ethers there are formed ether acetals which are then transformed into $\alpha, \beta$-unsaturated aldehydes by the following scheme [1, 2]:

$$RCH=CHCH(OR)_2 \xrightarrow{CH_2=CHOR} RCH=CH-CH-CH_2-CH(OR)_2 \longrightarrow$$
$$\underset{OR}{|}$$

$$\longrightarrow RCH=CH-CH=CHCHO \xrightarrow{(RO)_3CH} RCH=CH-CH=CH-CH(OR)_2 \xrightarrow{CH_3CH=CHOR}$$
$$\underset{CH_3}{|}$$

$$\longrightarrow RCH=CH-CH=CH-CH-CH-CH(OR)_2 \longrightarrow RCH=CH-CH=CH-CH=C-CHO$$
$$\underset{OR}{|} \qquad\qquad\qquad \underset{CH_3}{|}$$

Use of vinyl ethyl and propenyl ethyl esters permits one to grow the polyene chain by two and three carbon atoms with introduction of one double bond.
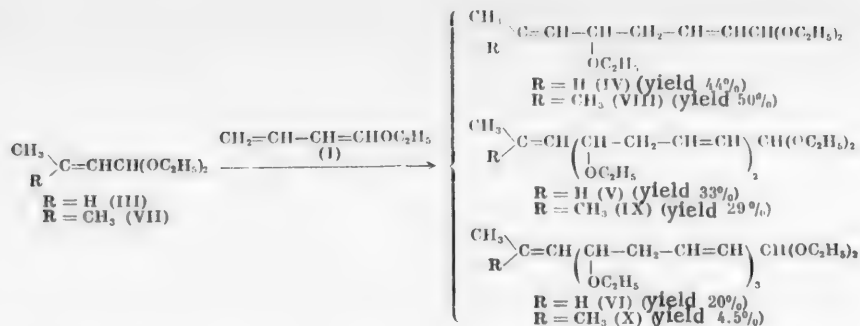
We decided to use in the synthesis of polyene aldehydes the dienic ethers which had not been previously used for this purpose. For 1-alkoxydienes we selected 1-ethoxy-1,3-butadiene [3] (I) and ethoxyisoprene (3-methyl-1-ethoxy-1,3-butadiene) (II) which had been recently synthesized in our laboratory [4]. The use of ethoxyisoprene would permit one to lengthen the polyene chain by 5 carbon atoms at once, with introduction of 2 double bonds and a methyl group into the position necessary for the isoprenoids.

As expected, the condensation of acetals of $\alpha, \beta$-unsaturated aldehydes with ethoxybutadiene and ethoxyisoprene proceeded readily under the influence of zinc chloride or boron trifluoride. The acetals add to ethoxybutadiene and ethoxyisoprene in 1,4-position; thereby are formed, in high yields, the corresponding $\alpha, \beta$-unsaturated ether acetals, which are then smoothly converted, depending on the reaction conditions, to ether aldehydes and polyeneals.
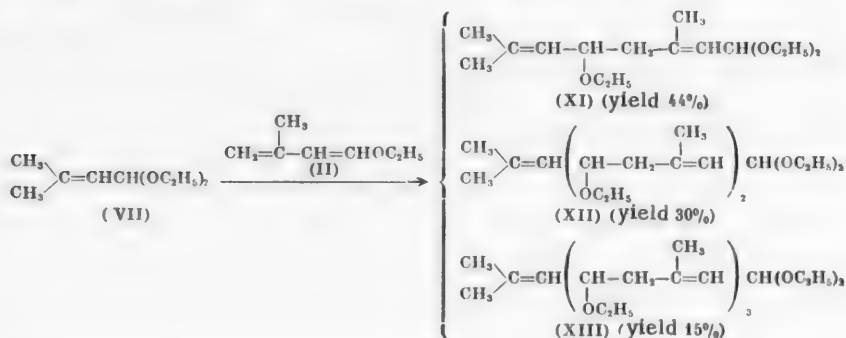
In the reaction of the acetal of crotonaldehyde (III) with ethoxybutadiene (I), under the influence of boron trifluoride at the temperature of 0-5°, there was obtained in the total yield of 97% a mixture of the ether acetals (IV), (V) and (VI) (see diagram at top of following page).

Formation of ether acetal (V) is explained by the fact that the resulting, from the reaction, ether acetal (IV) is in turn added to a second molecule of ethoxybutadiene. Ether acetal (VI) is formed analogously from ether acetal (V) and ethoxybutadiene. From ether acetal (IV), isolated in pure state, and ethoxybutadiene there were obtained, in the presence of boron trifluoride ethereate, the ether acetals (V) and (VI) in yields of 38% and 36%, respectively. As the result of the condensation of the acetal of dimethylacrylaldehyde (VII) with ethoxybutadiene, under the influence of boron trifluoride ethereate at 0-5° or zinc chloride at 60-65°, there was obtained a mixture of ether acetals (VIII), (IX) and (X), in the total yield of 83.5%. In the condensation of ether acetal (VIII) with

$$
\begin{array}{c}
CH_3 \\
R
\end{array}
\!\!>\!\!C=CHCH(OC_2H_5)_2
\quad\xrightarrow[\;(I)\;]{\;CH_2=CH-CH=CHOC_2H_5\;}\quad
\left\{
\begin{array}{l}
\begin{array}{c}CH_3\\R\end{array}\!\!>\!\!C=CH-CH-CH_2-CH=CHCH(OC_2H_5)_2 \\
\qquad\qquad\qquad\; \overset{\textstyle |}{OC_2H_5} \\
\qquad R = H\ (IV)\ \text{(yield 44\%)} \\
\qquad R = CH_3\ (VIII)\ \text{(yield 50\%)} \\[4pt]
\begin{array}{c}CH_3\\R\end{array}\!\!>\!\!C=CH\!\left(\!\begin{array}{c}CH-CH_2-CH=CH\\ \overset{\textstyle |}{OC_2H_5}\end{array}\!\right)_{\!2}\!\!CH(OC_2H_5)_2 \\
\qquad R = H\ (V)\ \text{(yield 33\%)} \\
\qquad R = CH_3\ (IX)\ \text{(yield 29\%)} \\[4pt]
\begin{array}{c}CH_3\\R\end{array}\!\!>\!\!C=CH\!\left(\!\begin{array}{c}CH-CH_2-CH=CH\\ \overset{\textstyle |}{OC_2H_5}\end{array}\!\right)_{\!3}\!\!CH(OC_2H_5)_2 \\
\qquad R = H\ (VI)\ \text{(yield 20\%)} \\
\qquad R = CH_3\ (X)\ \text{(yield 4.5\%)}
\end{array}
\right.
$$

$$
\begin{array}{c}
CH_3\\R
\end{array}
\!\!>\!\!C=CHCH(OC_2H_5)_2 \\
R = H\ (III) \\
R = CH_3\ (VII)
$$

ethoxybutadiene there were formed ether acetals (IX) and (X), in yields of 22.5 and 32%, respectively. Ethoxy-
isoprene (II) enters the reactions with the acetals even more readily than does ethoxybutadiene. In the reaction
of acetal (VII) with ethoxyisoprene (II), under the influence of zinc chloride at room temperature, there was ob-
tained in the total yield of 89% a mixture of ether acetals (XI), (XII) and (XIII).

$$
\begin{array}{c}
CH_3\\CH_3
\end{array}
\!\!>\!\!C=CHCH(OC_2H_5)_2
\quad\xrightarrow[\;(II)\;]{\;CH_2=\overset{\textstyle CH_3}{\underset{}{C}}-CH=CHOC_2H_5\;}\quad
\left\{
\begin{array}{l}
\qquad\qquad\qquad\quad \overset{\textstyle CH_3}{|} \\
\begin{array}{c}CH_3\\CH_3\end{array}\!\!>\!\!C=CH-CH-CH_2-C=CHCH(OC_2H_5)_2 \\
\qquad\qquad\qquad\; \overset{\textstyle |}{OC_2H_5} \\
\qquad\qquad (XI)\ \text{(yield 44\%)} \\[6pt]
\begin{array}{c}CH_3\\CH_3\end{array}\!\!>\!\!C=CH\!\left(\!\begin{array}{c}\overset{\textstyle CH_3}{|}\\ CH-CH_2-C=CH\\ \overset{\textstyle |}{OC_2H_5}\end{array}\!\right)_{\!2}\!\!CH(OC_2H_5)_2 \\
\qquad\qquad (XII)\ \text{(yield 30\%)} \\[6pt]
\begin{array}{c}CH_3\\CH_3\end{array}\!\!>\!\!C=CH\!\left(\!\begin{array}{c}\overset{\textstyle CH_3}{|}\\ CH-CH_2-C=CH\\ \overset{\textstyle |}{OC_2H_5}\end{array}\!\right)_{\!3}\!\!CH(OC_2H_5)_2 \\
\qquad\qquad (XIII)\ \text{(yield 15\%)}
\end{array}
\right.
$$

( VII )

In the condensation of ether acetal (XI) with ethoxyisoprene under the same conditions there were formed
ether acetals (XII) and (XIII) in yields of 41 and 25%, respectively.

The reactions of acetals with ethoxydienes, as shown by our experiments, do not proceed singularly: as the
result of the reaction there is formed a mixture of ether acetals, which are the products of addition of one, two
or three molecules of the ethoxydiene to the acetal. The formation of ether acetals with high molecular weight
is explained by the fact that as the result of addition of the unsaturated acetal to ethoxydiene there is formed
again an unsaturated ether acetal, which enters sufficiently readily into a reaction with a second molecule of
the ethoxydiene, etc. In order that the main reaction products be ether acetals formed as the result of addition
of one or two molecules of ethoxydiene to the acetal, it is necessary to use the excess of the acetal. The effect
of the excess acetal (VII) on the yield of the resulting ether acetals is evident in the example of condensation of
acetal (VII) with ethoxyisoprene (II) under the influence of zinc chloride (see Table below).

We also realized the condensation of acetal (VII) with vinyl ethyl ether. In this case we used equimolar
amounts of the acetal (VII) and the vinyl ethyl ether, and nevertheless obtained only one ether acetal (XIV) in

| Acetal (VII) (g) | Ethoxyiso-prene (II) in g | Molar ratio (VII) : (II) | Ether acetal (VIII) | | Ether acetal (IX) | | High-boiling ether acetals and residue (in g) |
|---|---|---|---|---|---|---|---|
| | | | g | % | g | % | |
| 9.9 | 7.0 | 1 : 1 | 2.2 | 13 | 1.5 | 12.6 | 4.9 |
| 14.0 | 6.6 | 1.5 : 1 | 5.5 | 35 | 3.2 | 28.5 | 2.8 |
| 23.2 | 6.6 | 2.5 : 1 | 7.0 | 44 | 2.9 | 26.0 | 2.5 |
| 37.2 | 6.6 | 4 : 1 | 7.5 | 47 | 3.8 | 34.0 | 2.0 |

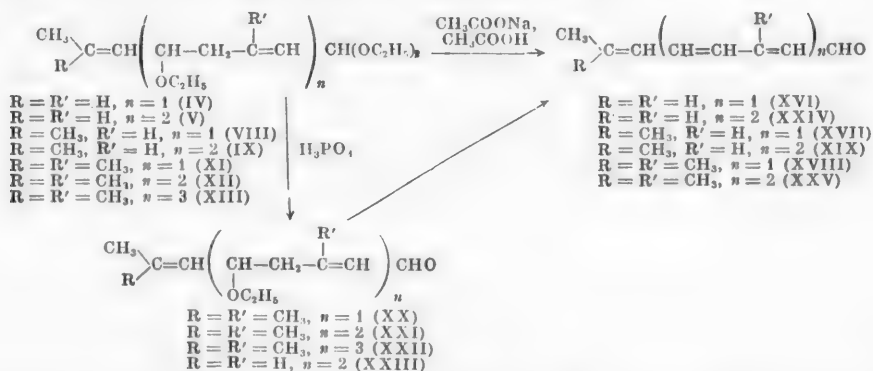the yield of 71%, this being converted then into 2-methyl-2,4-hexadien-6-al (XV).

$$\underset{\text{(VII)}}{\overset{CH_3}{\underset{CH_3}{>}}C=CH-CH(OC_2H_5)_2} \xrightarrow[71\%]{CH_2=CHOC_2H_5}$$

$$\longrightarrow \underset{\underset{\text{(XIV)}}{\overset{|}{OC_2H_5}}}{\overset{CH_3}{\underset{CH_3}{>}}C=CH-CH-CH_2-CH(OC_2H_5)_2} \xrightarrow{\text{(yield 90\%)}} \underset{\text{(XV)}}{\overset{CH_3}{\underset{CH_3}{>}}C=CH-CH=CHCHO}$$
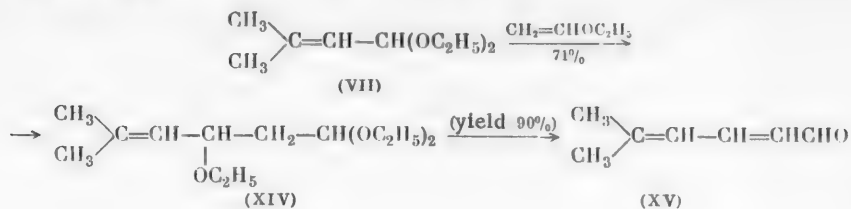
The singularity of course of the reaction in this case is evidently explained by the fact that the rate of addition of the unsaturated acetal (VII) to vinyl ethyl ether is greater than the rate of addition of the resulting saturated ether acetal (XIV).

Ether acetals, resulting from the condensation of acetals of $\alpha,\beta$-unsaturated aldehydes with ethoxydienes, are quite stable compounds which are distillable in vacuo of 0.1 mm without decomposition and their separation does not present any difficulties. The ether acetals were converted in high yield into polyene aldehydes by heating with a mixture of sodium acetate and acetic acid (Isler method). In this manner there were prepared: 2,4,6-octatrien-8-al (XVI) from ether acetal (IV) (yield 88%); 2-methyl-2,4,6-octatrien-8-al (XVII) from ether acetal (VIII) (yield 95%); dehydrocitral (XVIII) from ether acetal(XI) (yield 89%) and 2-methyl-2,4,6,8,10-dodecapentaen-12-al (XIX) from ether acetal (IX) (yield 72%).

We found that ether acetals are quantitatively hydrolyzed to ether aldehydes under the influence of 1% orthophosphoric acid.

From ether acetals (XI), (XII), (XIII),and (V) there were obtained 4-ethoxycitral (XX), 4,8-diethoxyfarnesal (XXI), 2,6,10,14-tetramethyl-4,8,12-triethoxy-2,6,10,14-hexadecatetraen-16-al (XXII) and 4,8-diethoxy-2,6,10-dodecatrien-12-al (XXIII).

The ether aldehydes are readily converted to polyenals by the action of p-toluenesulfonic acid in toluene. By this method there were prepared 2,4,6,8,10-dodecapentaen-12-al (XXIV) and farnesal (XXV) from ether aldehydes (XXI) and (XXIII); these substances could not be prepared directly from the ether acetals (V) and (XII). 4-Ethoxycitral (XX) was converted in 92% yield into dehydrocitral (XVIII).

$$\underset{R}{\overset{CH_3}{>}}C=CH\left(\underset{\underset{OC_2H_5}{|}}{CH-CH_2-\overset{\overset{R'}{|}}{C}=CH}\right)_n CH(OC_2H_5)_2 \xrightarrow{\underset{CH_3COOH}{CH_3COONa,}} \underset{R}{\overset{CH_3}{>}}C=CH\left(CH=CH-\overset{\overset{R'}{|}}{C}=CH\right)_n CHO$$

R = R′ = H, n = 1 (IV)  
R = R′ = H, n = 2 (V)  
R = CH₃, R′ = H, n = 1 (VIII)  
R = CH₃, R′ = H, n = 2 (IX)  
R = R′ = CH₃, n = 1 (XI)  
R = R′ = CH₃, n = 2 (XII)  
R = R′ = CH₃, n = 3 (XIII)

|H₃PO₄

R = R′ = H, n = 1 (XVI)  
R = R′ = H, n = 2 (XXIV)  
R = CH₃, R′ = H, n = 1 (XVII)  
R = CH₃, R′ = H, n = 2 (XIX)  
R = R′ = CH₃, n = 1 (XVIII)  
R = R′ = CH₃, n = 2 (XXV)

$$\underset{R}{\overset{CH_3}{>}}C=CH\left(\underset{\underset{OC_2H_5}{|}}{CH-CH_2-\overset{\overset{R'}{|}}{C}=CH}\right)_n CHO$$

R = R′ = CH₃, n = 1 (XX)  
R = R′ = CH₃, n = 2 (XXI)  
R = R′ = CH₃, n = 3 (XXII)  
R = R′ = H, n = 2 (XXIII)

All polyenals, except (XVII) were obtained in a crystalline form. Aldehydes (XVI), (XXIV) and (XVIII) had melting points corresponding to the literature data [5-7] and did not give a depression in mixed melting with the corresponding aldehydes isolated previously by us from the polyene condensation of crotonaldehyde and dimethylacrylaldehyde under the effect of piperidine acetate; the melting point of (XXV) corresponded to the literature data [7]. Polyenals (XIX) and (XVII) were prepared for the first time and the latter was subjected to exhaustive hydrogenation to 2-methyloctanal, the melting point of whose 2,4-dinitrophenylhydrazone agreed with the literature data [8].

Condensation of acetals of $\alpha,\beta$-unsaturated aldehydes with ethoxyisoprene and ethoxybutadiene is a new and convenient method of synthesis of polyene aldehydes.

## EXPERIMENTAL

Condensation of diethyl acetal of crotonaldehyde (III) with ethoxybutadiene (I). To a mixture of 24 g of acetal (III) and 0.12 g of boron trifluoride etherate, cooled to 0°, there was added over 1.5 hr with mechanical stirring under a nitrogen atmosphere 11 g of ethoxybutadiene (I). The mixture was stirred for 3.5 hrs at 0-10°, was then diluted with ether, washed with 5% solution of sodium hydroxide, water, dried with potassium carbonate and distilled in vacuo.

The following substances were isolated.

1) 7 g of unreacted acetal (III) with b. p. 66-70° (25 mm), $n^{22}D$ 1.4120.

2) 12 g of 4,8,8-triethoxy-2,6-octadiene (IV).

B. p. 59-61° (0.09 mm), $n^{20}D$ 1.4435, $d_4^{20}$ 0.9026, MR 71.22; calc. 70.84. Found %: C 69.95, 69.82; H 10.74, 10.97. $C_{14}H_{26}O_3$. Calculated %: C 69.40; H 10.73.

3) 6.4 g of 4,8,12,12-tetraethoxy-2,6,10-dodecatriene (V).

B. p. 105-110° (0.05 mm), $n^{20}D$ 1.4555, $d_4^{20}$ 0.9245, MR 100.0; calc. 99.73. Found %: C 70.90, 70.82; H 10.81, 10.63. $C_{20}H_{36}O_4$. Calculated %: C 70.60; H 10.58.

4) 3.4 g of 4,8,12,16,16-pentaethoxy-2,6,10,14-hexadecatetraene (VI).

B. p. 140-145° (0.05 mm), $n^{20}D$ 1.4610, $d_4^{20}$ 0.9344, MR 128.8; calc. 128.62. Found %: C 71.45, 71.11; H 10.72, 10.54. $C_{26}H_{46}O_5$. Calculated %: C 71.20; H 10.57.

Condensation of 4,8,8-triethoxy-2,6-octadiene (IV) with ethoxybutadiene (I). By the above described method there was obtained from 19 g of ether acetal (IV), 3.85 g of ethoxybutadiene (I) and 0.05 g of boron trifluoride etherate, 10.5 g of unreacted ether acetal (IV), 5.1 g of ether acetal (V) and 3.1 g of ether acetal (VI).

2,4,6-Octatrien-1-al (XVI). A mixture of 3.3 g of ether acetal (IV), 1.1 g of sodium acetate, 0.7 ml of water and 11 ml of acetic acid were stirred for 4.5 hrs (95°) in a stream of nitrogen. The reaction mixture, after cooling, was poured into 30 g of ice and the resulting oil was extracted with petroleum ether. The extract was washed with 5% solution of sodium bicarbonate and water and was dried with calcined magnesium sulfate. After distillation under nitrogen there was obtained 1.45 g of a yellow liquid with b. p. 54-56° (0.1 mm) which crystallized after cooling. After two recrystallizations from petroleum ether there was isolated 2,4,6-octatrien-1-al in the form of cream colored crystals with m. p. 57.5-58.5°.

4,8-Diethoxy-2,6,10-dodecatrien-12-al (XXIII). A mixture of 5 g of ether acetal (V) and 2.5 ml of 10% orthophosphoric acid was heated with stirring under a nitrogen stream on a boiling water bath for 1.5 hr. After being cooled, the reaction mixture was diluted with ether, washed with 5% solution of sodium bicarbonate and water, dried and distilled in vacuo in a nitrogen stream. There was obtained 3.4 g of ether aldehyde (XXIII) in the form of a yellowish liquid.

B. p. 91-94° (0.03 mm), $n^{20}D$ 1.4675, $d_4^{20}$ 0.9448. Found %: C 72.26, 72.05; H 10.04, 10.08. $C_{16}H_{26}O_3$. Calculated %: C 72.15; H 9.84.

2,4,6,8,10-Dodecapentaen-12-al (XXIV). A mixture of 3.4 g of ether aldehyde (XXIII), 60 ml of absolute toluene and 30 mg of p-toluenesulfonic acid were heated under nitrogen in a Wood metal bath at bath temperature of 125-130°. A slow distillation of toluene with alcohol took place. At the same time toluene was added to the flask to maintain a constant volume of the reaction mixture. The distillation of alcohol stopped after 1 hr (test for alcohol content in the distillate was made according to Chugaev-Tserevitinov). The reaction mixture was cooled, washed with 5% solution of sodium bicarbonate and water, dried and distilled in vacuo under a nitrogen stream. There was obtained 1.4 g of substance with b. p. 105-110° (0.1 mm) which began to crystallize during the distillation. After recrystallization from petroleum ether, then from methanol, there were isolated yellow crystals of 2,4,6,8,10-dodecapentaen-12-al (XXIV) with m. p. 158-160°.

<u>Condensation of diethyl acetal of dimethylacrylaldehyde (VII) with ethoxybutadiene (I).</u> To a mixture of 15 g of acetal (VII) and 0.1 g of boron trifluoride etherate, cooled to 0°, there was added with mechanical stirring in a stream of nitrogen over 30 min, 6.2 g of ethoxybutadiene (I). Then the reaction mixture was stirred for 3.5 hrs at 0-10° and was subjected to the usual treatment. After vacuum distillation there were isolated the following substances:

1) 4.8 g of original acetal (VII) with b. p. 53-63° (16 mm), $n^{18.5}D$ 1.4220.

2) 8.1 g of 2-methyl-4,8,8-triethoxy-2,6-octadiene (VIII) in the form of a colorless mobile liquid.

B. p. 80-82° (0.02 mm), $n^{20}D$ 1.4476, $d_4^{20}$ 0.9036, MR 75.9; calc. 75.46. Found %: C 70.30, 69.99; H 10.95, 11.05. $C_{15}H_{28}O_3$. Calculated %: C 70.40; H 10.93.

3) 3.3 g of 2-methyl-4,8,12,12-tetraethoxy-2,6,10-dodecatriene (IX) in the form of a slightly yellowish liquid.

B. p. 126-130° (0.02 mm), $n^{20}D$ 1.4595, $d_4^{20}$ 0.9264, MR 104.7; calc. 104.34. Found %: C 71.43, 71.36; H 10.74, 10.82. $C_{21}H_{38}O_4$. Calculated %: C 71.20; H 10.73.

4) 0.3 g of 2-methyl-4,8,12,16,16-pentaethoxy-2,6,10,14-hexadecatetraene (X) in the form of a yellow viscous liquid.

B. p. 155-160° (0.02 mm), $n^{20}D$ 1.4670, $d_4^{20}$ 0.9371, MR 134.3; calc. 133.2. Found %: C 71.55, 71.68; H 10.62, 10.60. $C_{27}H_{48}O_5$. Calculated %: C 71.64; H 10.69.

<u>Condensation of 2-methyl-4,8,8-triethoxy-2,6-octadiene (VIII) with ethoxybutadiene (II).</u> To a mixture of 10 g of ether acetal (VIII) and 0.04 g of boron trifluoride etherate, cooled to 0°, there was added with stirring over 30 min 3.8 g of ethoxybutadiene. After 4 hrs at 0-8°, the reaction mixture was subjected to the above described treatment. After vacuum distillation at 0.06 mm, there was obtained 3.8 g of ether acetal (VIII) which had failed to react, 3.1 g of ether actal (IX) and 2.8 g of ether acetal (X). Residue, 3.3 g.

<u>2-Methyl-2,4,6-octatrien-8-al (XVII).</u> A mixture of 5.6 g of ether acetal (VIII), 1.8 g of sodium acetate, 1.1 ml of water and 17.5 ml of acetic acid was heated in nitrogen stream at 95° with mechanical stirring for 4.5 hrs. After the usual treatment, the product was vacuum distilled in a stream of nitrogen. There was obtained 2.8 g of 2-methyl-2,4,6-octatrien-8-al (XVII) with b. p. 63-64° (0.02 mm). Aldehyde (XVII) was an uncrystallizing yellow liquid with the odor of 2,4,6-octatrien-8-al (XVI). The 2,4- dinitrophenylhydrazone of aldehyde (XVII) melted at 204-205° (from a mixture of chloroform and methanol).

$\lambda_{max}$ in isooctane 321, 396.5 m$\mu$. Found %: N 17.81, 17.76. $C_{15}H_{16}O_4N_4$. Calculated %: N 17.73.

<u>2-Methyl-2,4,6,8,10-dodecapentaen-12-al (XIX).</u> A mixture of ether acetal (IX; 3.4 g), 1.6 g of sodium acetate, 1 ml of water and 16 ml of acetic acid was heated at 95° in nitrogen stream for 5 hrs with mechanical stirring. After the usual treatment and vacuum distillation there was obtained 1.4 g of 2-methyl-2,4,6,8,10-dodecapentaen-12-al (XIX) with b. p. 100-105° (0.06 mm), which crystallized soon to a yellow crystalline mass. After two recrystallizations from ethyl alcohol, the aldehyde (XIX) was isolated in the form of golden yellow leaflets with m. p. 136-137°.

$\lambda_{max}$ (in ethanol) 234.5 m$\mu$ (log $\epsilon$ 3.96), 271.5 m$\mu$ (log $\epsilon$ 3.97), 391 m$\mu$ (log $\epsilon$ 4.67). Found %: C 83.50, 83.33; H 8.68, 8.33. $C_{13}H_{16}O$. Calculated %: C 83.00; H 8.52.

<u>Condensation of diethyl acetal of dimethylacrylaldehyde (VII) with ethoxyisoprene (II).</u> To a mixture of 204 g of acetal (VII) and 13 ml of 10% solution of zinc chloride in ethyl acetate there was added over 2.5 hrs at 20° with stirring 35.6 g of ethoxyisoprene; the temperature rose thereupon to 27°. Then the reaction mixture was stirred for 1.5 hr at room temperature and 45 min at 35-40°, after which it was diluted with ether, washed with 5% solution of sodium hydroxide and water, dried with potassium carbonate and vacuum distilled. The following products were isolated:

1) 159 g of the initial acetal (VII) with b. p. 65-68° (24 mm), $n^{18}D$ 1.4215.

2) 38.0 g of 2,6-dimethyl-4,8,8-triethoxy-2,6-octadiene (XI) in the form of a colorless liquid.

B. p. 80-81° (0.1 mm), $n^{20}D$ 1.4517, $d_4^{20}$ 0.9120, MR 79.82; calc. 80.08. Found %: C 71.28, 71.20; H 11.10, 11.11. $C_{16}H_{30}O_3$. Calculated %: C 71.08; H 11.19.

3) 18.0 g of 2,6,10-trimethyl-4,8,12,12-tetraethoxy-2,6,10-dodecatriene (XII).

B. p. 124-126° (0.04 mm), $n^{20}$D 1.4618, $d_4^{20}$ 0.9200, MR 114.3; calc. 113.59. Found %: C 72.24, 72.26; H 10.91, 10.91. $C_{23}H_{42}O_4$. Calculated %: C 72.18; H 11.06.

4) 7.8 g of 2,6,10,14-tetramethyl-4,8,12,16,16-pentaethoxy-2,6,10,14-hexadecatetraene (XIII) in the form of a yellowish viscous liquid.

B. p. 164-168° (0.07 mm), $n^{20}$D 1.4710, $d_4^{20}$ 0.9298. Found %: C 73.00, 72.84; H 11.04, 10.84. $C_{30}H_{54}O_5$. Calculated %: C 72.85; H 11.00.

Condensation of 2,6-dimethyl-4,8,8-triethoxy-2,6-octadiene (XI) with ethoxyisoprene (II). By the above described method there was prepared from 12 g of ether acetal (XI), 2.5 g of ethoxyisoprene and 0.6 ml of 10% solution of zinc chloride in ethyl acetate, 7.8 g of the initial ether acetal (XI), 3.45 g of ether acetal (XII) and 1.4 g of ether acetal (XIII).

4-Ethoxycitral (XX). A mixture of 8.1 g of ether acetal (XI), 1 g of 1% orthophosphoric acid and 2.5 ml of ethyl alcohol was stirred in a stream of nitrogen for 1.5 hrs at room temperature. The reaction mixture became homogeneous after 15 min. The mixture was diluted with ether, washed with 5% solution of sodium bicarbonate and water, dried with magnesium sulfate and distilled in vacuum in nitrogen atmosphere. There was obtained 5.3 g of 4-ethoxycitral (XX) in the form of colorless (yellowing on standing) liquid which did not smell of lemon peel.

B. p. 58-60° (0.06 mm), $n^{20}$D 1.4762, $d_4^{20}$ 0.9247, MR 59.89; calc. 58.34. $\lambda_{max}$ (in ethanol) 240 mμ (log$\epsilon$ 4.132), 326 mμ (log $\epsilon$ 1.956). Found %: C 73.29, 73.46; H 10.10, 9.98. $C_{12}H_{20}O_2$. Calculated %: C 73.41; H 10.27.

Dehydrocitral (XVIII). a) A mixture of 3.2 g of 4-ethoxycitral (XX), 50 ml of absolute toluene and 5 mg of p-toluenesulfonic acid was heated in a nitrogen stream on a Wood metal bath at bath temperature of 110-130°. A slow distillation of toluene and alcohol took place; after 20 min the distillation of alcohol ceased (test for alcohol content in the distillate made with Chugaev-Tserevitinov method). The reaction mixture was cooled and washed with 5% solution of sodium bicarbonate and water, dried with magnesium sulfate and distilled in vacuo in nitrogen atmosphere. There was obtained 2.25 g of dehydrocitral (XVIII) with b. p. 57-60° (0.05 mm) which crystallized on cooling. After two recrystallizations from petroleum ether there were isolated the light yellow crystals of (XVIII) with m. p. 39-40°.

b) A mixture of 10 g of ether acetal (XI), 3.2 g of sodium acetate, 2 ml of water and 30 ml of acetic acid was heated to 95° in nitrogen stream with stirring for 5 hrs. After the usual treatment and distillation, there was obtained 4.8 g of dehydrocitral (XVIII) with b. p. 64-65° (0.06 mm), m. p. 39-40° (from petroleum ether).

2,6,10-Trimethyl-4,8-diethoxy-2,6,10-dodecatrien-12-al (4,8-diethoxyfarnesal) (XXI). A mixture of 6.5 g of ether acetal (XII), 0.75 g of 1% orthophosphoric acid and 1.75 ml of ethyl alcohol was shaken in a closed flask at room temperature. The layers disappeared after 10 min; after further 1.5 hrs the mixture was subjected to the usual treatment and vacuum distillation in nitrogen atmosphere. There was obtained 5.02 g of 4,8-diethoxyfarnesal (XXI) in the form of a yellowish liquid.

B. p. 114-115° (0.04 mm), $n^{20}$D 1.4875, $d_4^{20}$ 0.9419, MR 94.28; calc. 91.84. Found %: C 73.99, 74.13; H 10.43, 10.44. $C_{19}H_{32}O_3$. Calculated %: C 73.98; H 10.46.

Farnesal (XXV). A mixture of 2 g of undistilled 4,8-diethoxyfarnesal (XXI), 50 ml of absolute toluene and 6 mg of p-toluenesulfonic acid was heated in nitrogen atmosphere in a Wood metal bath at bath temperature of 120-125°. A slow distillation of toluene and alcohol took place and simultaneously with this distillation toluene was gradually added to the flask so as to maintain a constant volume of the mixture. After 1 hr the distillation of alcohol ceased (test for alcohol content in the distillate was made according to Chugaev-Tserevitinov). After the usual treatment and vacuum distillation in nitrogen atmosphere there was obtained 0.85 g of substance with b. p. 115-120° (0.05 mm), which began to crystallize during the distillation. After two recrystallizations there was isolated farnesal (XXV) in the form of yellow leaflets with m. p. 119-120° (from ethyl alcohol).

$\lambda_{max}$ (in ethanol), 239 mμ (log $\epsilon$ 3.92), 279 mμ (log $\epsilon$ 3.97), 386 mμ (log $\epsilon$ 3.99). Found %: C 83.40; H 9.41. $C_{15}H_{20}O$. Calculated %: C 83.23; H 9.32.

2,6,10,14-Tetramethyl-4,8,12-triethoxy-2,6,10,14-hexadecatetraen-16-al (XXIII). A mixture of 3 g of ether acetal (XIII), 0.75 g of 1% orthophosphoric acid and 1.75 ml of ethyl alcohol was shaken in a closed flask at room temperature. After 1.5 hr the mixture was subjected to the usual treatment. There was obtained 1.9 g of ether aldehyde (XXIII) in the form of a viscous yellow liquid.

B. p. 158-162° (0.1 mm), $n^{20}D$ 1.4954, $d_4^{20}$ 0.9452. Found %: C 74.06, 74.30; H 10.24, 10.20. $C_{26}H_{54}O_6$. Calculated %: C 74.27; H 10.54.

Condensation of diethyl acetal of dimethylacrylaldehyde (VII) with vinyl ethyl ether. To a mixture of 6.4 g of acetal (VII) and 1 ml of 10% solution of zinc chloride in ethyl acetate, heated to 55-60°, there was added over 30 min with stirring 3.2 g of vinyl ethyl ether. The mixture was heated for 4 hrs at 60° and was then distilled in vacuo. There was obtained 6.6 g of 2-methyl-4,6,6-triethoxy-2-hexene (XIV).

B. p. 63-65° (0.01 mm), $n^{20}D$ 1.4295, $d_4^{20}$ 0.8906, MR 66.73; calc. 66.70. Found %: C 68.08, 67.90; H 11.15, 11.23. $C_{13}H_{26}O_3$. Calculated %: C 67.85; H 11.3.

2-Methyl-2,4-hexadien-6-al (XV). A mixture of 10.4 g of ether acetal (XIV), 3.7 g of sodium acetate, 2.5 ml of water and 36 ml of acetic acid was heated at 95° in nitrogen atmosphere with stirring for 4 hrs. After the usual treatment and vacuum distillation there was obtained 4.4 g of 2-methyl-2,4-hexadien-6-al (XV).

B. p. 90-91° (23 mm), $n^{20}D$ 1.5541, $d_4^{20}$ 0.9036. $\lambda_{max}$ (in methanol) 285 m$\mu$ (log $\epsilon$ 4.46). Found %: C 76.34, 76.18; H 9.26, 9.22. $C_7H_{10}O$. Calculated %: C 76.3; H 9.09.

The 2,4-dinitrophenylhydrazone of the aldehyde (XV) has m. p. 200-202° (from a mixture of methyl alcohol and ethyl acetate).

$\lambda_{max}$ (in heptane) 266.5, 303, 379.5 m$\mu$. Found %: N 19.31, 19.45. $C_{13}H_{14}O_4N_4$. Calculated %: N 19.32.

## SUMMARY

Condensation of acetals with ethoxyisoprene and ethoxybutadiene was realized for the first time.

The use of ethoxyisoprene permits one to lengthen a carbon chain by 5 carbon atoms with introduction of 2 double bonds and an aldehyde group conjugated to them (in case of addition of one molecule of ethoxyisoprene) as well as by 10 carbon atoms with introduction of 4 double bonds (in case of addition of 2 molecules of ethoxyisoprene), which represents the new and simple method of synthesis of polyene aldehydes of the isoprenoid type.

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# SYNTHESIS OF DIENIC ACIDS FROM α-PYRONES

## L. I. Kudriashov and N. K. Kochetkov

Recently we described a simple and convenient method of synthesis of esters of α-pyrone-3-carboxylic acids [1] from β-chlorovinyl ketones. The present paper describes the experiments directed toward the utilization of the indicated α-pyrone-3-carboxylic acid for the preparation of difficultly accessible aliphatic acids and their derivatives.

With this as a goal we first examined the hydrogenation of derivatives of α-pyrone. We succeeded in showing that α-pyrone-3-carboxylic acids and their esters are smoothly hydrogenated over palladium on barium sulfate and are transformed into the corresponding α-carboxy (or α-carbethoxy)-δ-lactones (yield: 70-85%).



(I) $R = CH_3$, $R' = H$; (II) $R = CH_3$, $R' = C_2H_5$; (III) $R = C_5H_{11}$, $R' = C_2H_5$.
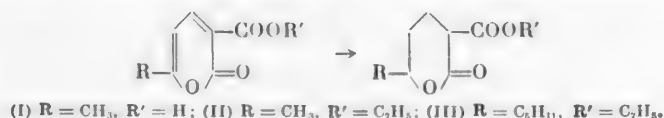
It should be noted that the hydrogenation proceeds rather slowly, which is not unexpected since it is well known that α-pyrones show some of the symptoms of aromaticity. In order to avoid the processes connected with hydrogenolysis of the resulting δ-lactone, it was rational to stop the hydrogenation shortly before the uptake of 2 moles of hydrogen.

Then we studied the bromination of the resulting α-carbethoxy (or α-carboxy)-δ-lactones for solution of the problem of the possible preparation of unsaturated δ-lactones by a subsequent dehydrobromination. Since the compounds (I)-(III), prepared by us, are cyclic analogs of malonic acid and its derivatives, the bromination was accomplished under mild conditions. The bromination of the lactone of α-carboxy-δ-hydroxycaproic acid (I) was accompanied by decarboxylation, which complicated the reaction. Bromination of the appropriate esters, specifically lactones of α-carbethoxy-δ-hydroxycaproic (II) and -decanoic (III) acids can be accomplished by the action of bromine in the presence of pyridine. However, the isolation of the resulting bromides is connected with great difficulties since they partly lose the elements of hydrogen bromide during distillation and for this reason cannot be isolated in an analytically pure state. Owing to this, it is rational to run the dehydrobromination without isolating the bromides in a pure state.

At first we attempted to accomplish the transformation of the thus obtained α-bromo-α-carbethoxy-δ-lactones into the corresponding α,β-unsaturated δ-lactones, to which belongs a series of physiologically active substances parasorbic acid, massoya lactone). However, all attempts to dehydrobrominate the above bromides were accompanied by more complex changes connected with the opening of the lactone ring. More interesting was the result obtained on treatment of the indicated bromides with diethylaniline with heating. As the result of this reaction there were isolated esters of the corresponding α,β,γ,δ-doubly unsaturated aliphatic acids — sorbic and 2,4-decadienoic acids.



$$\rightarrow R-CH=CH-CH=CH-COOC_2H_5,$$

$$R = CH_3, C_5H_{11}$$
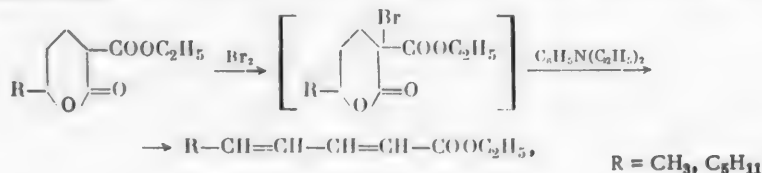
The mechanism of this interesting transformation was not clarified by us, but it is easy to think that in it there first takes place a dehydrobromination, followed by ring opening and decarboxylation. Transformations of a similar type, which proceed at high temperatures, are known in the series of $\beta$-lactones [2], and our compounds are vinylogs of such substances. The presence of a tertiary amine in this case must aid ring opening. An attempt to realize the loss of hydrogen bromide by the action of aqueous and alcoholic solutions of potassium hydroxide failed to give the desired results. A study of the reaction products formed thereby showed that in this case there takes place a replacement of bromine by hydroxy and methoxy groups instead of the cleavage of hydrogen bromide.

The path of preparation of difficultly accessible dienic acids with a conjugated bond system, discovered by us, has an undoubted preparative interest when one considers the accessibility of the initial 3-carbethoxy-$\alpha$-pyrones and the good yields. Esters of dienic acids were hydrolyzed by us to the corresponding acids. The thus obtained sorbic and 2,4-decadienoic acid corresponded to the trans-trans isomers by their constants. It is impossible to say whether or not the esters prepared during the treatment with diethylaniline were also trans-trans isomers, since their hydrolysis can be accompanied by isomerization [3].

In conclusion it should be noted that the dienoic acids prepared by us can be readily converted into the corresponding $\alpha, \beta$-unsaturated $\delta$-lactones [4], which can thus be prepared from the corresponding $\alpha$-pyrones by a somewhat more complex route than proposed by us at first.

## EXPERIMENTAL

Lactone of $\alpha$-carboxy-$\delta$-hydroxycaproic acid. A suspension of 10.0 g (0.065 mole) of 6-methyl-$\alpha$-pyrone-3-carboxylic acid in 50 ml of ether was hydrogenated in the presence of 0.5 g of palladium on barium sulfate (palladium content 5%) until the uptake of 2.85 liters of hydrogen (0°, 760 mm). The catalyst was filtered off, ether was evaporated and the remaining oil crystallized partially after many days of drying in a vacuum desiccator. The crystals were pressed on a porous plate and recrystallized from a mixture of benzene and petroleum ether; yield, 7.15 g (69.6%); m. p. 75-76° (decomp.).

Found %: C 53.65, 53.61; H 6.62, 6.61. $C_7H_{10}O_4$. Calculated %: C 53.16; H 6.37.

The lactone of $\alpha$-carboxy-$\delta$-hydroxycaproic acid forms colorless crystals, soluble in water, alcohol, ether and benzene.

Lactone of $\alpha$-carbethoxy-$\delta$-hydroxycaproic acid. 6-Methyl-3-carbethoxy-$\alpha$-pyrone (23.1 g, 0.13 mole) was hydrogenated in 100 ml of alcohol over 2 g of palladium on barium sulfate (palladium content 5%) until the uptake of 4.9 liters (0.22 mole) of hydrogen (0°, 760 mm), after which the catalyst was filtered off, the alcohol distilled off and the residue was vacuum distilled collecting the fraction with b. p. 134-136° (4 mm); yield: 18.9 g (78%). After two distillations the substance had the following constants:

B. p. 119-120° (1 mm), $d_4^{20}$ 1.1311, $n^{20}D$ 1.4550, $MR_D$ 44.66; calc. 44.87. Found %: C 58.26, 58.25; H 7.68, 7.68. $C_9H_{14}O_4$. Calculated %: C 53.05; H 7.58.

The lactone of $\alpha$-carbethoxy-$\delta$-hydroxycaproic acid is a colorless oil, soluble in the majority of organic solvents.

Lactone of $\alpha$-carbethoxy-$\delta$-hydroxycapric acid. 6-Amyl-3-carbethoxy-$\alpha$-pyrone (38.5 g; 0.16 mole) was hydrogenated over 2.2 g of palladium on barium sulfate (palladium content 5%) in 50 ml of alcohol until the uptake of 6.9 liters of hydrogen (0.31 mole) (0°, 760 mm). The catalyst was then filtered off, the alcohol was distilled and the residue vacuum distilled, collecting the fraction with b. p. 170-172° (6 mm); yield: 32.5 (84%). After two redistillations the substance had the following constants:

B. p. 170-172° (6 mm), $d_4^{20}$ 1.0429, $n^{20}D$ 1.4561, $MR_D$ 63.09; calc. 63.34. Found %: C 64.09, 64.10; H 9.14, 9.32. $C_{13}H_{22}O_4$. Calculated %: C 64.43; H 9.15.

The lactone of $\alpha$-carbethoxy-$\delta$-hydroxycapric acid was an oily liquid with a characteristic odor, soluble in the usual organic solvents.

Sorbic acid. To a solution of 1.68 g (0.09 mole) of the lactone of $\alpha$-carbethoxy-$\delta$-hydroxycaproic acid in 30 ml of anhydrous carbon tetrachloride there was added slowly with cooling and stirring 15.8 g (0.08 mole)

of N-bromosuccinimide, after which the mixture was heated for 2 hrs at 55°. On the following day the precipitated succinimide was filtered off, the filtrate was evaporated and the residue distilled in vacuum, collecting the fraction which boiled with strong decomposition at 149-152° (3 mm); yield, 4.7 g. In all the following redistillations, a strong decomposition was observed with formation of insignificant amounts of a lower boiling fraction. A mixture of 12 g of the resulting bromide and 23 g of freshly distilled diethylaniline was heated on an oil bath for 1 hr at the bath temperature of 130-140°; after cooling, the mixture was diluted with absolute ether, the diethylaniline hydrobromide was filtered off, washed with absolute ether, the ethereal solution washed with 10% solution of hydrochloric acid for the removal of diethylaniline (4 times with 100 ml), dried over magnesium sulfate and vacuum distilled for the isolation of the ethyl ester of sorbic acid; yield, 4.5 g (37%); b. p. 74-76° (14 mm). The ether ester of sorbic acid (3.7 g, 0.026 mole) was boiled for 30 min with 20 ml of 20% aqueous solution of sodium hydroxide, then was treated with enough water to dissolve the sodium sorbate which had precipitated during the saponification, extracted twice with ether and the aqueous layer, after the separation of ether, was sucked with a stream of air pulled with a water pump for 20 min to remove traces of residual ether, acidified, the precipitated sorbic acid being filtered off, and dried in vacuo over phosphoric anhydride; yield 1.9 g (64.4%); m. p. 132-133° (from water).

Found %: C 64.14, 64.15; H 7.30, 7.28. $C_6H_8O_2$. Calculated %: C 64.27; H 7.19.

Literature data [3]: trans-trans-sorbic acid, m. p. 134.5°.

Ethyl ester of 2,4-decadienoic acid. To a solution of 15.5 g (0.07 mole) of $\alpha$-carbethoxy- $\delta$ -hydroxycapric acid in 30 ml of anhydrous carbon tetrachloride there was added 6 ml of dry pyridine, after which there was slowly added, with cooling and stirring, a solution of 3.8 ml of bromine in 25 ml of carbon tetrachloride. After completion of bromine addition, the pyridine hydrobromide was filtered off, the mother liquor was evaporated in vacuo from a water pump and to the residue there was added 22 ml of diethylaniline; the mixture was heated for 1 hr on an oil bath at 135-140°; on cooling, the reaction mixture was diluted with absolute ether, the precipitated diethylaniline hydrobromide was filtered off and washed with absolute ether, the ether was distilled from the filtrate and the residue was vacuum distilled, collecting the fraction with b. p. 106-115° (5 mm). The crude product containing some diethylaniline was dissolved in 50 ml of ether, washed with 10% hydrochloric acid (3 times 25 ml), twice with water, the ethereal layer removed and dried over magnesium sulfate and freed of ether by distillation; the residual ethyl ester of 2,4-decadienoic acid was vacuum distilled, collecting the fraction with b. p. 108-110° (5 mm); yield, 3.5 g (28%). After two distillations, the product had the following constants:

B. p. 109-110° (5 mm), $d_4^{20}$ 0.9155, $n^{20}D$ 1.4720. Found %: C 73.29, 73.40; H 10.53, 10.45. $C_{12}H_{20}O_2$. Calculated %: C 73.43; H 10.27.

2,4-Decadienoic acid. Ethyl ester of 2,4-decadienoic acid (2.1 g; 0.011 mole) was boiled for 30 min with 10 ml of 20% aqueous solution of potassium hydroxide and 5 ml of methanol. After cooling, there was added 20 ml of water, extracted twice with ether, the aqueous layer was acidified and extracted with ether (3 times 20 ml), the ethereal extracts were dried with magnesium sulfate, freed of ether by distillation and the residue was vacuum distilled, collecting the fraction with b. p. 144-147° (3 mm); yield, 1.3 g (73%). After two distillations the substance had the following constants:

B. p. 144-145° (2 mm), $n^{20}D$ 1.4938. Found %: C 71.24, 71.13; H 9.70, 9.45. $C_{10}H_{16}O_2$. Calculated %: C 71.39; H 9.59.

The benzylthiuronium salt was prepared as usual; m. p. 167°.

Found %: N 8.07, 8.10. $C_{18}H_{26}O_2N_2S$. Calculated %: N 8.38.

Literature data [5]: for trans-trans-2,4-decadienoic acid: $n^{20}D$ 1.4918; benzylthiuronium salt, m. p. 175°.

## SUMMARY

1. It was shown that $\alpha$-carbethoxy-$\delta$ -lactones are formed in high yield during the hydrogenation of 6-alkyl-3-carbethoxy-$\alpha$-pyrones.

2. A new method of preparation of aliphatic dienic acids was developed by the way of bromination of corresponding $\alpha$-carbethoxy-$\delta$ -lactones with a subsequent treatment of the bromides with diethylaniline.

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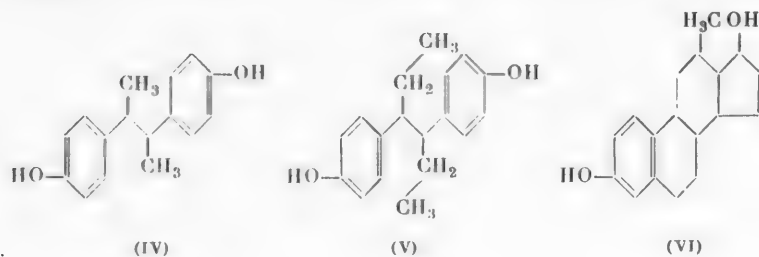
# DIPHENSUCCINDANE AND 2,6-DIHYDROXYDIPHENSUCCINDANE

S. F. Torf and N. V. Khromov-Borisov

Steroidal hormones are derivatives of cyclopentanophenanthrene (I). Diphensuccindane (indano-2',1': 1,2-indane) (II) has some elements of structural similarity to (I). * Therefore, the synthesis and the study of the corresponding derivatives has points of interest in the search for new synthetic medicinal substances, as well as in the study of the link between the chemical structure and the pharmacological action in this series of compounds.
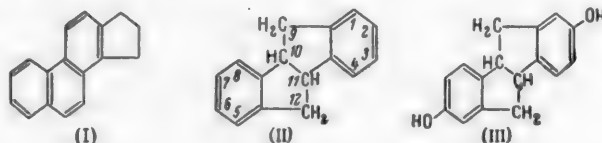


We synthesized several derivatives of diphensuccindane, among which we    describe      in this paper the synthesis of diphensuccindane itself and of its 2,6-dihydroxy derivative (III).

It is known that p,p'-dihydroxy derivatives of diphenylethane hydrocarbons, containing alkyl radicals at the ethane carbon atoms, possess some estrogenic properties. The most active in this respect are p,p-dihydroxymeso-2,3-diphenylbutane (IV) [1] and p,p-dihydroxy-meso-3,4-diphenylhexane (synestrol) (V) [1]. The high estrogenic activity of the latter is explained in part by its structural similarity to estradiol (VI) [1] — natural hormone, having high estrogenic activity.



2,6-Dihydroxydiphensuccindane (III) is a closed analog of p,p'-dihydroxy-2,3-diphenylbutane (IV) and in its tetracyclic structure possesses a greater degree of similarity to estradiol than does p,p'-dihydroxy-2,3-diphenylbutane.

Over 20 papers have been published in the literature, relative to the derivatives of diphensuccindane, mainly substituted in positions 9, 10, 11 or 12. Among the derivatives substituted in the benzene rings, there have been described 2,6-dinitrodiphensuccindanedione (VII) [2] and 2,6-diaminodiphensuccindanedione (VIII) [2] (see diagram at top of following page).

The 2- and 6-positions of nitro groups in 2,6-dinitrodiphensuccindanedione were assigned on the basis of the following data. By oxidation of this dinitro product [2] there was obtained in 57% yield 4-nitrophthalic acid;

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* In the present paper we do not consider the stereoisomerism of these compounds.
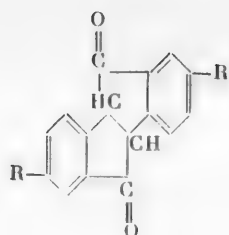
(VII)   R = NO$_2$
(VIII)  R = NH$_2$
(IX)    R = H

the same acid may be obtained in the oxidation of 3,7-dinitrodiphensuccindanedione. However, the 3- and 7-positions of the nitro groups are excluded by the authors [2] on the basis of the meta-orienting effect of keto groups in the nitration of the diphensuccindanedione (IX).

The first derivative of diphensuccindane series — diphensuccindanedione (IX) was prepared by Reimer [3]. The structure of this derivative was later established by Roser [4] without a clarification of the spatial configuration.

We prepared diphensuccindanedione by Reimer's method [3], by heating meso-diphenylsuccinic acid [5] with sulfuric acid, but at lower temperature [6]. Diphensuccindanedione was also prepared by us from the racemate of diphenylsuccinic acid [5] but, as already noted in the literature [4], the yield of diphensuccindanedione in this case was considerably lower.

The synthesis of 2,6-dihydroxydiphensuccindanedione, starting with diphensuccindanedione was conducted as follows: diphensuccindanedione was converted by the previously described method [2] into 2,6-dinitrodiphensuccindanedione and further into 2,6-diaminodiphensuccindanedione [2]. The experiments run by us with the reduction of 2,6-diaminodiphensuccindanedione by the Clemmensen method for the preparation of 2,6-diaminodiphensuccindane (X) failed to give positive results. Therefore (VIII) was at first acetylated, then reduced by Clemmensen method to 2,6-diacetamidodiphensuccindane (XI), from which the 2,6-diaminodiphensuccindane was obtained after hydrolysis. 2,6-Dihydroxydiphensuccindane was prepared from the latter compound by diazotization reaction and further decomposition of the diazo compound.

It should be noted that during boiling of the diamino product (VIII) with excess acetic anhydride until the precipitate dissolved, there was formed a tetraacetyl derivative. This was isolated and analyzed by us, but its structure was not studied in more detail. This compound may have the structure of 2,6-bis-(diacetylamino)diphensuccindanedione (XII) or 2,6-diacetylamino-9,12-diacetoxydiphensuccindanedione (XIII). Two acetyl are cleaved on boiling this compound with aqueous acetic acid.
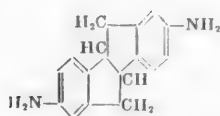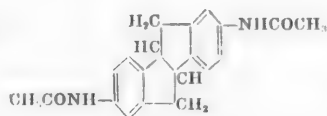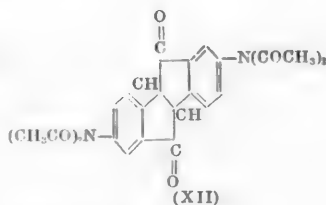


(X)   (XI)   (XII)
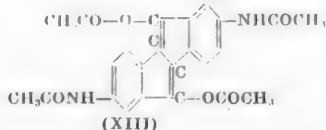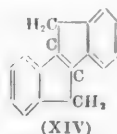
(XIII)   (XIV)

For a further study of the properties of diphensuccindane (II) we developed a convenient method of its preparation from diphensuccindanedione (IX). In the literature there is described a synthesis of diphensuccindane by the way of reaction of diphensuccindanedione with phosphorus and hydroiodic acid [4], as well as by catalytic reduction of diphensuccindene (XIV) [7], prepared in two steps from diphensuccindanedione [7]. We prepared diphensuccindane by reduction of diphensuccindanedione by Clemmensen method in sulfuric acid medium with simultaneous distillation of the reaction products with steam.

Tests of estrogenic properties of 2,6-dihydroxydiphensuccindane, made by A. I. Podlesnaia, showed that this compound has insignificant estrogenic activity (1000 $\gamma$ per mouse in 54% of cases). Thus, in the strength of its estrogenic action 2,6-dihydroxydiphensuccindane is considerably closer to the racemate of p,p'-dihydroxy-2,3-diphenylbutane (1000 $\gamma$ per rat in 100% of cases) than to its stereoisomer p,p'-dihydroxy-meso-2,3-diphenylbutane (0.5 $\gamma$ [1], 10 $\gamma$ [1] per rat in 100% of cases).

It is interesting to note that 2,8-dihydroxy-5,6,11,12,13,14-hexahydrochrysene (XV) described in the literature [8], which in its structure is a closed analog of p,p'-dihydroxy-3,4-diphenylhexane is in the strength of its estrogenic action (1000 $\gamma$ per rat in 100% of cases [1, 8]) also closer to the racemate of p,p'-dihydroxy-3,4-diphenylhexane (XVI) (500 $\gamma$ [1], 1000 $\gamma$ [1] per rat in 100% of cases) than to p,p'-dihydroxy-meso-3,4-diphenylhexane (synestrol) (V) (0.2 $\gamma$ per rat in 100% of cases [1]).



(XV)      (XVI)
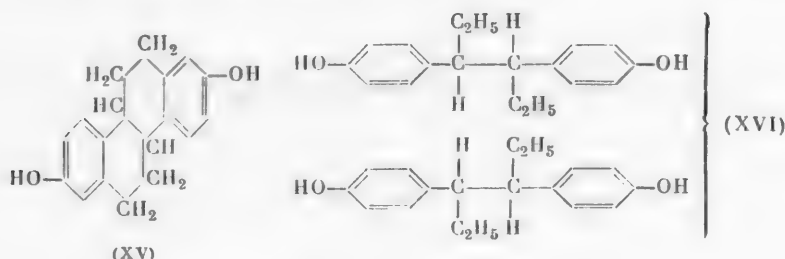
## EXPERIMENTAL

Diphensuccindanedione.  To 320 ml of concentrated sulfuric acid there was added 75 g of meso-diphenylsuccinic acid, after which the mixture was stirred and heated for 20-30 min at 110°. The resulting brown solution was stirred at 110° for 10 min longer, then poured in a stream into a 2-liter beaker half-filled with ice. After several hours, the precipitate was filtered off and washed with water. The weight of the precipitate, dried at 50°, was 29 g. After recrystallization from 1400 ml of alcohol there was obtained 22 g of diphensuccindanedione with m. p. 204-206°, the product being colorless. From the mother liquor, after the distillation of the main bulk of alcohol, there was isolated an additional 3 g of the substance with yellow color and m. p. 203-205°. Yield 38.5%.

In some experiments the product precipitated in the form of very fine and difficulty filterable solid. For facilitation of filtration, the precipitate along with the liquid, was heated for 40 min on a boiling water bath, as the result of which the precipitate was coarsened and was filtered without difficulty. The yield in these cases reached 50%.

It should be noted that diphensuccindanedione (m. p. 204-206°), recrystallized from alcohol, contains insignificant amounts of a higher melting impurity which has acid properties. The impurity is detected by observation of the melting of the substance under a microscope on a hot stage [9]. For the removal of this impurity from the main substance, 50 g of diphensuccindanedione was dissolved in 300 ml of dioxane at 95-100° and the hot solution was poured in a thin stream into 450 ml of 1.5% aqueous solution of potassium carbonate with energetic stirring. A precipitate of diphensuccindanedione forms thereby while the liquid shows an alkaline reaction to phenolphthalein. After stirring for 40 min, the mixture was set aside for several hours after which the precipitate was filtered off, washed with water and dried at 100°. The thus purified diphensuccindanedione (48.6 g) melted in a capillary at 203-205° (uncorrected), while on a hot stage it melted at 208-209°, and it melted homogeneously. For preparation of diphensuccindanedione from the racemate of diphenylsuccinic acid, purified through the barium salt and recrystallized from water, the yield reaches but 8.7%. The mixed melting point with diphensuccindanedione prepared from meso-diphenylsuccinic acid gave no depression.

2,6-Dinitrodiphensuccindanedione.  20 g of diphensuccindanedione was added over 40 min to a solution of 40 g of potassium nitrate in 216 ml of concentrated sulfuric acid at 3-8°. After this the stirring was continued for 3 hrs without cooling, whereupon the temperature of the solution rose to 18°. The solution was poured on ice, the resulting precipitate was filtered off, washed with water and dried at 50°. Weight, 27.6 g. The precipitate was boiled for one hour with dilute acetic acid (75 ml of acetic acid and 75 ml of water), and the undissolved portion was filtered off while hot, boiled with 200 ml of acetic acid for one hour, the mixture was then treated

with 30 ml of water, the mixture boiled for 30 min longer, the undissolved precipitate filtered off while hot, washed with hot dilute acetic acid and dried at 100°. The weight of 2,6-dinitrodiphensuccindanedione was 10.9 g (35.7%), m. p. 239-241°, yellowing at 236°. The precipitate was recrystallized from 300 ml of ethylene chloride. After cooling of the filtrate in a freezing mixture there was obtained 9.6 g of product which was colorless and had a flesh shade; m. p. 239-241°. Additional 1 g of product with m. p. 239-241° was isolated after distillation of the bulk of the solvent.

Found %: N 8.43, 8.34. $C_{16}H_8O_6N_2$. Calculated %: N 8.64.

2,6-Diaminodiphensuccindanedione. A mixture of 10 g of 2,6-dinitrodiphensuccindanedione, 22.5 g of granulated tin and 132 ml of concentrated hydrochloric acid was heated for 6 hrs on a boiling water bath. Then the mixture was refluxed for 20-40 min until the small residual precipitate had dissolved. The mixture of liquid and precipitate, obtained after cooling, was saturated with hydrogen chloride, with water cooling. On the following day, the precipitate was filtered off on a porous glass filter, washed with concentrated hydrochloric acid, dissolved in dilute hydrochloric acid (300 ml of water and 12 ml of concentrated hydrochloric acid), the tin was precipitated from it with hydrogen sulfide and the filtrate was evaporated to dryness.

The residue was dissolved in dilute hydrochloric acid (150 ml of water and 4 ml of concentrated hydrochloric acid) and the filtered solution was poured into excess dilute ammonium hydroxide. A very fine, difficultly filterable precipitate formed. After standing for 4 hrs, the precipitate was filtered off, washed with water and dried at 100°. The weight of 2,6-diaminodiphensuccindanedione was 6.2 g (76%); light yellow (lemon) colored solid, which did not melt at 325°.

Found %: N 10.50, 10.60. $C_{16}H_{12}O_2N_2$. Calculated %: N 10.60.

Tetraacetyl derivative (XII) or (XIII). A mixture of 1 g of 2,6-diaminodiphensuccindanedione and 65 ml of acetic anhydride was refluxed for 4-5 hrs until the precipitate had dissolved. The precipitate did not reform on cooling the solution. From the yellow solution, the acetic anhydride was distilled in vacuo from a boiling water bath. The dry residue was dissolved at room temperature in 20 ml of chloroform, the chloroform solution was filtered from a precipitate (0.15 g), which did not melt at 300°, and the filtrate was gradually diluted with 80 ml of petroleum ether. The resulting precipitate was filtered off. The weight of the air-dried residue was 1.5 g. This precipitate was refluxed with 30 ml of dry benzene, the solution was filtered from a slight precipitate (0.07 g) while warm and the slightly warm solution was diluted with an equal volume of petroleum ether. The resulting precipitate was filtered off. The weight of air-dry tetraacetyl derivative was 1.15 g (70.1%); it changes at 210°, m. p. 218-220°. It has a flesh color.

Found %: C 66.42, 66.24; H 4.88, 4.77; N 6.38, 6.79. $C_{24}H_{20}O_6N_2$. Calculated %: C 66.67; H 4.66; N 6.48.

2,6-Diacetylaminodiphensuccindane (XI). A mixture of 5.2 g of 2,6-diaminodiphensuccindanedione and 300 ml of acetic anhydride was refluxed for 5 hrs until the precipitate had dissolved. On the following day 25 g of zinc dust was stirred for 15 min with a solution of 7 ml of acetic acid and 120 ml of water, the solution was decanted, the remaining zinc was stirred for 15 min with 25 ml of 5% solution of mercuric chloride, after which the metal was filtered off, washed several times with water and the wet precipitate of amalgamated zinc was added to the above-described solution of the tetraacetyl derivative in acetic anhydride. The solution was heated to boiling and to the boiling solution there was added 150 ml of water over 2 hrs. The addition of water through the reflux condenser was done at first in very small portions — 1-3 ml each, since after each such addition the mixture boiled up energetically. After completion of addition of water, the mixture was refluxed for 4 hrs longer. On the following day the precipitate which had formed overnight was dissolved by heating. The solution was refluxed for 5 hrs longer, while 150 ml of water was being added during the first 2 hrs. The hot mixture was filtered from the zinc residue (3.3 g). The resulting precipitate after cooling of the mixture was separated and washed with dilute acetic acid, then was stirred with water, filtered and dried. Its weight was 3.2 g. The precipitate was recrystallized from 50 ml of acetic acid. There was obtained 3.1 g (49.2%) of 2,6-diacetylaminodiphensuccindane, dried at 110°; it was white with a grey shade. M. p. 238-241°.

Found %: N 8.42, 8.55. $C_{20}H_{20}O_2N_2$. Calculated %: N 8.74.

2,6-Diaminodiphensuccindane (X). A mixture of 3 g of 2,6-diacetylaminodiphensuccindane, 300 ml of water and 20 ml of concentrated hydrochloric acid was refluxed with stirring in a flask of 1500 ml capacity (the

mixture foams) for about 15 hrs until the precipitate had dissolved; the heating was done with interruptions while stirring was employed only during the first half of heating since the bumping of the precipitate ceased gradually. Then the solution was refluxed with 1 g of activated carbon and the hot filtrate was poured into dilute solution of alkali. The precipitate was filtered off after cooling. The weight of the precipitate, dried at 60°, was 1.55 g. The precipitate was dissolved with heating in 30 ml of alcohol (a small amount of impurity failed to dissolve), after which 80 ml of water was added and the mixture was boiled with activated carbon, filtered while hot, and the filtrate cooled with ice. The resulting precipitate was filtered off and dried at 100°. The temperature during drying was raised gradually to avoid fusing of the precipitate. There was obtained 1.1 g (50%) of the precipitate of 2,6-diaminodiphensuccindane, which was colorless; m. p. 134-136°.

Found %: C 81.16, 81.21; H 6.80, 7.27; N 11.82, 11.70. $C_{16}H_{16}N_2$. Calculated %: C 81.32; H 6.83; N 11.86.

2,6-Dihydroxydiphensuccindane (III). A mixture of 0.45 g of 2,6-diaminodiphensuccindane, 280 ml of water and 1 ml of concentrated sulfuric acid was stirred at 50° until the precipitate dissolved. The solution was cooled to room temperature; a precipitate formed thereupon. This mixture was diazotized with a solution of 0.27 g of sodium nitrite in 15 ml of water until a positive test with starch-iodide paper remained for 40 min. The resulting solution was warmed for 1.5 hrs on a boiling water bath. The solution at first turned cloudy, then gave a precipitate. On the following day there was added to the reaction mixture 2.5 g of potassium hydroxide, the mixture was stirred at room temperature until the precipitate dissolved and the filtered solution was poured into a solution of dilute hydrochloric acid. The resulting flesh colored precipitate was filtered off and dried at 60°; weight, 0.42 g; m. p. 221-222°. The precipitate was dissolved with heating in 100 ml of benzene and the solution was boiled with carbon, after which the warm filtrate was diluted with 160 ml of petroleum ether. On the following day, the resulting precipitate was filtered off. The weight of the dry precipitate of 2,6-dihydroxydiphensuccindane was 0.25 g (59.5%); it was colorless and had m. p. 222-224°.

Found %: C 81.02, 80.80; H 5.84, 6.24. $C_{16}H_{14}O_2$. Calculated %: C 80.65; H 5.92.

Diphensuccindane (II). 80 g of zinc dust was stirred for 10 min with 20 ml of water and 40 ml of concentrated hydrochloric acid; the mixture was transferred into a long-necked 2-liter flask, the zinc dust was washed with water by decantation, then was shaken for 10 min with 80 ml of 5% solution of mercuric chloride and 4 ml of concentrated hydrochloric acid; the solution of mercuric chloride was then decanted and the amalgamated zinc was washed with water by decantation. Then 20 g of diphensuccindanedione was added to the flask, along with a solution of 700 ml of water and 80 ml of concentrated sulfuric acid and the flask contents were steam distilled over 16-18 hrs (with interruptions). The liquid volume in the reaction flask was maintained at 800-900 ml. The reaction product mainly settled on the condenser walls and was pushed out, as it accumulated, from the condenser by means of a piece of cotton and a rod. The steam distilled product contained an admixture of mercury droplets and some zinc; the last portions of the distilled product had a reddish brown color. After recrystallization from 110 ml of alcohol there was obtained 9.5 g (54%) of diphensuccindane which was colorless and had m. p. 100-102°. From the alcoholic mother liquor part of the alcohol was distilled until about 60 ml remained. On cooling, there formed an additional 2 g of precipitate with m. p. 99-100°.

Found %: C 93.30, 93.56; H 6.90, 6.87. $C_{16}H_{14}$. Calculated %: C 93.16; H 6.84.

## SUMMARY

1. Diphensuccindane (by a new method) and 2,6-dihydroxydiphensuccindane were synthesized.

2. The estrogenic properties of 2,6-dihydroxydiphensuccindane and its open analog — p,p'-dihydroxy-2,3-diphenylbutane (meso form and racemate) were compared.

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# STUDIES IN THE SERIES OF ISOQUINOLINE COMPOUNDS

## XIV. ESTERS OF ISOMERIC 4',5'-DIMETHOXY-6-ETHYL-3,4,5,6,7,8-HEXAHYDROBENZO-(1,2:1',2')-QUINOLIZYL-7-ACETIC ACIDS

R. P. Evstigneeva

In the present paper there is described the preparation of esters of isomeric 4',5'-dimethoxy-6-ethyl-3,4, 5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acids which are important intermediates in the synthesis of isomeric emetines.

The synthesis was accomplished according to one [1] of the schemes previously suggested by us [2].

Fig. 1. Ultraviolet absorption spectra in ethyl alcohol. 1) Ethyl ester of N-[δ -(3',4'-dimethoxyphenyl)-ethyl]-δ -ethyl- α -piperidone- γ -acetic acid; 2) ethyl ester of δ -ethyl- α -piperidone-γ -acetic acid; 3) dihomoveratrylamine.
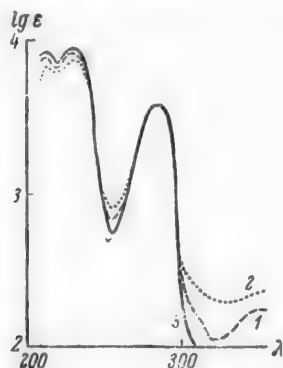


Fig. 2. Ultraviolet absorption spectra of hydrochlorides of ethyl esters of isomeric 4',5'-dimethoxy-6-ethyl-3,4,5, 6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acids in ethyl alcohol. Numbers of curves correspond to numbers of the isomers.

In the course of the synthesis there was prepared a series of esters of β -substituted glutaric acids (II-IV, R = CH₃).

The condensation of β -(α'-cyano)-propylglutaric acid (IV) with homoveratrylamine was studied in detail. Along with the main reaction product — the ester of N- [β -(3',4'-dimethoxyphenyl)-ethyl]-δ -ethyl-α-piperidone-γ -acetic acid (V) there were isolated the following by-products: 1) ester of δ -ethyl- α -piperidone- γ -acetic acid (VI) and 2) dihomoveratrylamine. The compounds prepared in this step have different ultraviolet absorption characteristics (Fig. 1).

The ester of N-[β -(3',4'-dimethoxyphenyl)-ethyl ]-δ -ethyl-α-piperidone-γ -acetic acid (V) may exist in principle in two isomeric forms; however, all our attempts to isolate a second isomer failed. Evidently, the substituent on the nitrogen aids the predominant formation of but one stereoisomer. According to the information gained from conformational analysis, the most advantageous structure for the substituted piperidone is the trans-form with equatorial substituents. The by-product, the ester of δ -ethyl- α -piperidone-γ -acetic acid which does not have any substituents at the nitrogen, is obtained under these conditions in two stereoisomeric forms: 1) crystalline cis-isomer, m. p. 84-85° and 2) liquid trans-isomer, b. p. 175-176° (1.5 mm).

The ester of N- [β -(3',4'-dimethoxyphenyl)-ethyl]-δ -ethyl-α-piperidone-γ -acetic acid is transformed by the action of phosphorus oxychloride into the derivative of quinolizine. The resulting salt of the quaternary base (VII) yields on reduction the ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (VIII). Hydrogenation of the chloride of the quaternary base proceeds stereospecifically, depending on the catalyst used and on the pH of the medium. As a result of this reaction there were isolated three compounds: 1) the isomer obtained during hydrogenation in the presence of platinum oxide in acid medium, 2) the isomer obtained during hydrogenation in the presence of platinum oxide in neutral medium, and 3) the isomer obtained in hydrogenation in the presence of Raney nickel in neutral medium.

In the case of hydrogenation with nickel with heating, isomerization evidently occurs. The resulting isomers are very close to each other in their properties but do display a depression in mixed melting points of their hydrochlorides. The isomers have almost coincident ultraviolet absorption spectra (Fig. 2).

### EXPERIMENTAL

I. Ethyl ester of N-[β -(3',4'-dimethoxyphenyl)-ethyl]-δ -ethyl- α -piperidone- γ -acetic acid (V, R = C₂H₅). Ethyl ester of β -(α'-cyano)-propylglutaric acid (10.42 g) and 48 g of homoveratrylamine in 50 ml of anhydrous ethyl alcohol were hydrogenated in the presence of 4 g of Raney nickel at 110 atmos and 110-115° for 1 hr. The catalyst was filtered off and the alcohol was distilled in vacuum. The residue was dissolved in benzene and washed with 3% hydrochloric acid, then with a sodium bicarbonate solution. After distillation of the solvent, the residue was distilled.

1st fraction. Ethyl ester of δ -ethyl- α -piperidone-γ -acetic acid (VI, R = C₂H₅). Yield: 0.75 g (8.66%). B. p. 169-170° (1 mm).

Found %: C 61.80; H 9.06; N 6.73. C₁₁H₁₉O₃N. Calculated %: C 61.95; H 8.98; N 6.57.

2nd fraction. Ethyl ester of N-[β-(3',4'-dimethoxyphenyl)-ethyl]-δ-ethyl-α-piperidone-γ-acetic acid (V, R = C$_2$H$_5$). Yield: 5.25 g (34.2%). B. p. 200.5-202.5° (0.15 mm).

Found %: C 66.79; H 8.26; N 3.77. C$_{21}$H$_{31}$O$_5$N. Calculated %: C 66.82; H 8.28; N 3.71.

Isolation of amines. The hydrochloric acid solution, obtained after the washing of the benzene extract of piperidones, was neutralized with alkali and extracted with benzene. After distillation of the solvent, the residue was distilled. There was obtained 33.6 g of homoveratrylamine taken for the reaction. The yield of dihomoveratrylamine was 2.74 g (6%). B. p. 198-205° (0.2 mm), m. p. 53.5-54°.

Methyl ester of N-[β-(3',4'-dimethoxyphenyl)-ethyl]-δ-ethyl-α-piperidone-γ-acetic acid (V, R = CH$_3$) was prepared analogously to the corresponding ethyl ester. Yield: 43.7%. B. p. 210-211° (0.35 mm).

Found %: C 65.80; H 7.91; N 4.11. C$_{20}$H$_{29}$O$_5$N. Calculated %: C 66.10; H 8.04; N 3.85.

As a by-product there was also obtained the unalkylated piperidone (VI, R = CH$_3$) in the yield of 5.71%. B. p. 112-115° (0.35 mm).

Found %: N 7.30. C$_{10}$H$_{17}$O$_3$N. Calculated %: N 7.02.

II. Methyl ester of β-(cyanocarbethoxy)-methylglutaric acid (II, R = CH$_3$) was obtained by the previously described method for the corresponding ethyl ester [1]. Yield: 82%.

B. p. 157-159° (2 mm), d$_4^{20}$ 1.1825, n$^{20}$D 1.4588, MR$_D$ 62.68; calc. 62.39. Found %: C 52.99; H 6.50; N 5.22. C$_{12}$H$_{17}$O$_6$N. Calculated %: C 53.13; H 6.31; N 5.16.

III. Methyl ester of β-(α'-cyano-α'-carbethoxy)-propylglutaric acid (III, R = CH$_3$) was prepared by the previously described method [1]. Yield: 86.5%.

B. p. 156-158° (1 mm), d$_4^{20}$ 1.1817, n$^{20}$D 1.4780, MR$_D$ 71.69; calc. 71.63. Found %: C 55.06; H 6.99; N 4.50. C$_{14}$H$_{21}$O$_6$N. Calculated %: C 56.18; H 7.07; N 4.69.

IV. Methyl ester of β-(α'-cyano)-propylglutaric acid (IV, R = CH$_3$) was prepared by the method, previously described for the ethyl ester [1]. The yield was 38%.

B. p. 126.5-127° (1 mm), d$_4^{20}$ 1.0912, n$^{20}$D 1.4506, MR$_D$ 56.00; calc. 56.12. Found %: C 58.12; H 7.56; N 6.29. C$_{11}$H$_{17}$O$_4$N. Calculated %: C 58.13; H 7.56; N 6.16.

V. Chloride of quaternary base of ethyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydro-9,10-dehydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (VII, R = C$_2$H$_5$). 1 g of ethyl ester of N-[β-(3',4'-dimethoxyphenyl)-ethyl]-δ-ethyl-α-piperidone-γ-acetic acid, 6 ml of anhydrous toluene, and 5.5 ml of phosphorus oxychloride were heated at gentle reflux for 1 hr. The toluene and excess phosphorus oxychloride were distilled off in vacuo. The residue was washed with 50 ml of absolute ether and was then dissolved in 10 ml of 6% hydrochloric acid. The solution was evaporated in vacuo at 25-30°. Complete removal of moisture was achieved by addition of anhydrous ethyl alcohol (5 ml, 3 times) to the residue and a subsequent distillation of it in vacuo. The residual red-yellow oil was the chloride of the quaternary base of the ethyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydro-9,10-dehydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid mixed with phosphoric acid.

VI. Ethyl esters of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acids (VIII, R = C$_2$H$_5$). 1. Hydrogenation in the presence of platinum oxide in acid medium. The crude chloride, prepared from 1 g of the piperidone, was dissolved in 7 ml of anhydrous ethyl alcohol and hydrogenated in the presence of 0.2 g of platinum oxide under 80 atmos for 4 hrs. The catalyst was filtered off and the alcohol was distilled off in vacuo. 10 ml of water was added to the residue. The solution was shaken with 20 ml of ether, then neutralized, with cooling, by means of aqueous ammonia. The separated oil was extracted with 50 ml of ether. The extract was washed with 10 ml of 5% aqueous alkali and dried with sodium sulfate. The base was a light yellow oil, readily soluble in the usual organic solvents and insoluble in water. The yield: 0.72 g (74.9%, calculated on the piperidone). The base distilled at 0.1 mm and the temperature of the air bath of 290-300°.

Found %: C 69.58; H 8.50; N 4.01. C$_{21}$H$_{31}$O$_4$N. Calculated %: C 69.78; H 8.65; N 3.87.

The hydrochloride was obtained in amorphous form by treatment of the ethereal solution of the base with ether containing hydrogen chloride. From the undistilled base, the hydrochloride separates in the form of a colorless amorphous substance, readily soluble in water and alcohol and insoluble in ether. It was very hygroscopic.

Found %: C 63.68; H 8.31; N 3.61. $C_{21}H_{32}O_4NCl$. Calculated %: C 63.38; H 8.11; N 3.52.

The hydrochloride prepared from distilled base was also amorphous and hygroscopic. M. p. 157-157.5°.

For the preparation of a crystalline hydrochloride, 0.5 g of the crude base ester was dissolved in 5 ml of 3% hydrochloric acid and evaporated in vacuo. The residue was taken up in the least volume of alcohol and treated with a few drops of ether until a slight cloudiness appeared. After a prolonged standing, the crystalline hydrochloride precipitated. Yield: 0.4 g. M. p. 196°. The hydrochloride crystallized with 1.5 molecule of water, owing to which the specimen was dried, prior to analysis, in vacuo at 110° for 1.5 hr.

Found %: C 63.40; H 8.19; N 3.78. $C_{21}H_{32}O_4NCl$. Calculated %: C 63.38; H 8.11; N 3.52.

The crystalline hydrochloride from the distilled base had m. p. 158-168°.

2. Hydrogenation in the presence of platinum oxide in neutral medium. The crude chloride, prepared from 1 g of the piperidone, was dissolved in 5 ml of anhydrous alcohol and neutralized with alcoholic solution of ammonia until the acid reaction to Congo red disappeared. The precipitate was separated and the filtrate was evaporated in vacuo. The residue was dissolved in 10 ml of anhydrous alcohol and subjected to hydrogenation at 110 atmos. After the usual treatment there was obtained 0.75 g (78.5%, based on piperidone) of the product. The hydrochloride was amorphous and had m. p. 171.5-173.5°. The crystalline hydrochloride was isolated analogously to the method described in the previous experiment; it gave colorless thin plates which formed rosettes. M. p. 194-196°. The substance was dried for 1.5 hr at 110° (1 mm) prior to the analysis.

Found %: C 63.54; H 8.16; N 3.59. $C_{21}H_{32}O_4NCl$. Calculated %: C 63.38; H 8.11; N 3.52.

3. Hydrogenation over Raney nickel. The chloride of quaternary base of the quinolizine, prepared from 2 g of the piperidone, was treated as in the previous experiment and hydrogenated in the presence of 1 g of Raney nickel at 100 atmos and 85-90° for 2 hrs. Yield: 0.95 g (49.6% based on the piperidone). The hydrochloride was amorphous; m. p. 175-179°. The crystalline hydrochloride formed thin colorless plates; m. p. 193.5-194.8°.

Found %: C 63.45; H 7.90; N 3.53. $C_{21}H_{32}O_4NCl$. Calculated %: C 63.38; H 8.11; N 3.52.

Below are shown the melting points of mixed samples of the isomers:

| Isomers | Amorphous hydrochlorides | Crystalline hydrates |
|---------|--------------------------|----------------------|
| 1 and 2 | 164.5-165.5° | 178-180° |
| 1 and 3 | 155-156° | 155-168° |
| 2 and 3 | 167-167.5° | 164-185° |

Methyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (VIII, R = $CH_3$) was isolated in 86.4% yield in the case of hydrogenation over Raney nickel catalyst. The amorphous hydrochloride had m. p. 186-187°. The crystalline hydrochloride was isolated in the form of irregular polyhedrons. M. p. 195-195.5°. The specimen was dried prior to analysis at 110° (1 mm) for 1.5 hr.

Found %: C 62.55; H 7.90; N 3.66. $C_{20}H_{30}O_4NCl$. Calculated %: C 62.54; H 7.88; N 3.65.

SUMMARY

1. The synthesis of esters of isomeric 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid was realized.

2. The reaction of condensation of methyl and ethyl esters of β-(α'-cyano)-propylglutaric acid with homoveratrylamine was studied.

3. The conditions for sterically directed hydrogenation of the quaternary chloride of the ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydro-9,10-dehydro-benzo-(1,2:1',2')-quinolizyl-7-acetic acid were worked out.

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• Original Russian pagination.  See C. B. translation.

# STUDIES IN THE SERIES OF ISOQUINOLINE COMPOUNDS

## XV. SYNTHESIS OF ISOMERIC o-METHYLPSYCHOTRINES

### R. P. Evstigneeva, R. G. Glushkov, and N. A. Preobrazhenskii

The alkaloid o-methylpsychotrine is isolated along with emetine from the roots of the tropical ipecacuanha plant. During the study of the alkaloids of this group the major attention was devoted to emetine since it possesses some valuable therapeutic properties and is contained in the plant in predominant amounts. The structure of emetine was established in 1949 [1-5] and confirmed by synthesis in 1950 [6]. The remaining ipecacuanha alkaloids have been studied less intensively and the structures of the majority of them have not been proved finally.

o-Methylpsychotrine was discovered only in 1917, considerably later than other alkaloids of this group. In its elemental composition o-methylpsychotrine differs from emetine only by a lesser content of hydrogen, by two atoms, and may be obtained from the latter by oxidation with mercuric acetate. o-Methylpsychotrine has been described as a secondary-tertiary base since it yields a singly substituted N-benzoyl derivative on being heated with benzoic anhydride. Formula (I) was suggested in 1927 for o-methylpsychotrine in accord with one of the structures proposed for emetine [7].
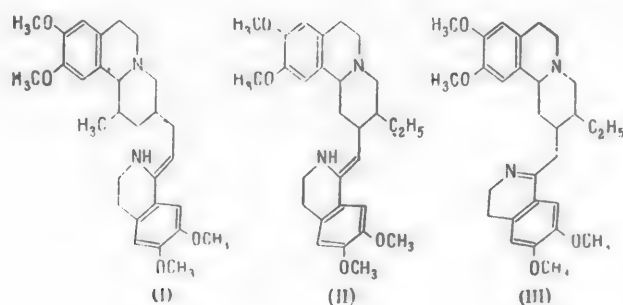


The position of the double bond was confirmed by the fact that in the oxidation of N-benzoyl-o-methyl-psychotrine with perphthalic acid and ozone there is obtained N-benzoylcoridaldine [8]. In 1949, following the establishment of emetine structure, formula (II) was accepted for o-methylpsychotrine. However, a little later a conclusion was drawn concerning the 1,2-position of the double bond in the dihydroisoquinoline ring (III) [9], on the basis of the study of the ultraviolet absorption spectrum of o-methylpsychotrine oxalate. However, this supposition is poorly compatible with the secondary-tertiary character of the base. Thus, the problem of the structure of o-methylpsychotrine remained open.

The scheme of emetine synthesis developed by us gave the opportunity to prepare o-methylpsychotrine as well. Stereoisomeric ethers of quinolizine (1-3) [17] were employed for this purpose (see diagram at top of next page).

Amides (V), which were close to each other in properties, were prepared by heating the esters (IV) with homoveratrylamine at 180-200°. The ultraviolet absorption maxima of these amides lie at the same wavelength (Fig. 1). The amides were converted into isoquinoline derivatives, which had the composition and the structure which corresponded to the alkaloid o-methylpsychotrine, the reaction being performed by the action of phosphorus
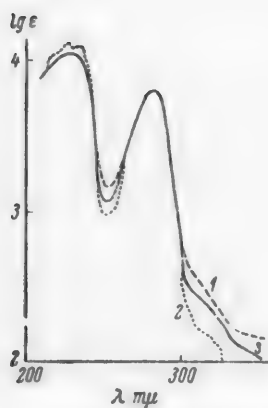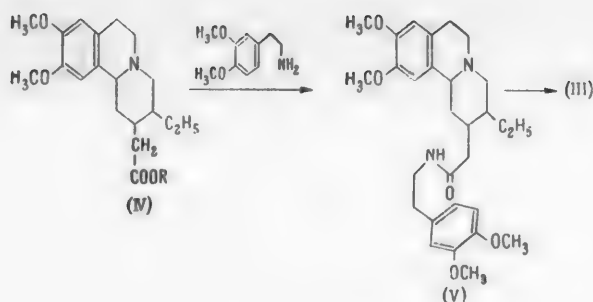
Fig. 1. Ultraviolet absorption spectra of the amides in ethyl alcohol. 1) Isomer 1; 2) isomer 2; 3) isomer 3.

oxychloride in chloroform solution. The bases were isolated in an amorphous state and had very close melting points. They were unstable to atmospheric oxygen and sunlight. Their oxalates were obtained in the form of crystalline hydrates which were readily recrystallized from methyl alcohol and lost water only after being dried at 110° and 1 mm for 3 hrs. The melting points of the oxalates were close to each other. The mixed melting points showed small but clear depressions. The (+)-tartrates were also prepared; these crystallize without water of crystallization.

The problem of the location of the double bond in 3,4-dihydro-isoquinoline ring remains unclear not only for o-methylpsychotrine but also for the entire group of similar compounds. On the basis of a study of the ultraviolet absorption spectra of 1-methyl-3,4-dihydro-6,7-methylenedioxyisoquinoline (VI), 1-benzyl-3,4-dihydro-6,7-methylenedioxyisoquinoline (VII) and 1-($\alpha$-picolyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline (VIII) and the comparison of these with the spectra of stilbene and $\alpha$-stilbazole Bills and Noller [10] concluded in favor of the exocyclic location of the double bond in 1-($\alpha$-picolyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline (VIII) and the endocyclic location of it in compounds (VI) and (VII).
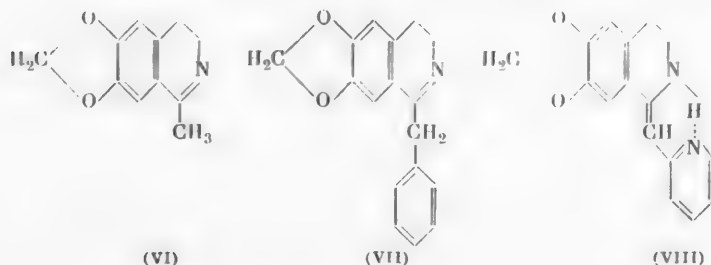


The character of the absorption curve changes in passing from the base (VIII) to the hydrochloride (IX), which fact is evidently connected with the translocation of the double bond. The exocyclic structure of compound (VIII) is explained, most probably, by the possibility of an intramolecular hydrogen bond (see diagram at top of next page).

This supposition is confirmed by the fact that 1-($\beta$-picolyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline, in which an intramolecular hydrogen bond cannot exist, has an endocyclic N=C double bond, as shown by the absorption spectrum and by transformation of compound (X) into the isoquinoline derivative (XI). 1-($\alpha$-Picolyl)-3,4-dihydro-6,7-methylenedioxyisoquinoline (VIII) does not yield an isoquinoline derivative.

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(IX)　　　　　(X)　　　　　(XI)
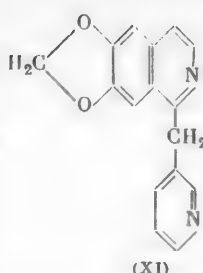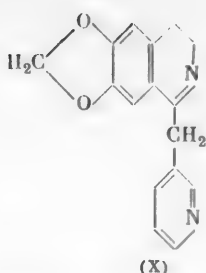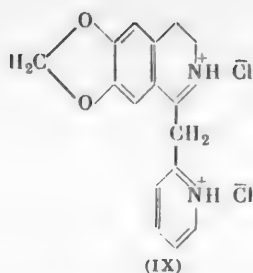
It is possible to conclude, on the basis of these studies, that for the 1-substituted 3,4-dihydroisoquinoline compounds the endocyclic location of the double bond is more common and that only in a few cases is the exocyclic disposition of the double bond possible.

Openshaw and Wood [9], in comparing the ultraviolet absorption spectra of the oxalate of natural o-methylpsychotrine with the spectrum of the hydrochloride of 1-methyl-3,4-dihydro-6,7-methylenedioxyisoquinoline, came to the conclusion of the endocyclic location of the double bond in o-methylpsychotrine. Although this position is correct in the final result, it could not be deduced solely on the basis of the spectrum of the salt. The spectroscopic study of the base was also necessary since the salt and the base might have different dispositions of the double bond.

We determined the ultraviolet spectra of the oxalates of the stereoisomeric synthetic o-methylpsychotrines (Fig. 2). The absorption curves of all three isomers coincide almost completely and are similar to the absorption curve of the oxalate of natural o-methylpsychotrine. The same is observed for the ultraviolet spectra of (+)-tartrates of o-methylpsychotrines (Figs. 2 and 3). We also examined the ultraviolet spectra of the stereoisomeric bases of o-methylpsychotrine isolated from the purified oxalates (Fig. 4). The absorption curves of the bases are similar to each other and are analogous in the maximum distribution to the absorption curves of 1-methyl- and 1-benzyl-3,4-dihydro-6,7-methylenedioxyisoquinolines.
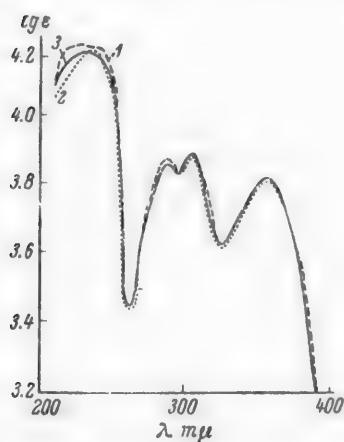
In accordance with these data the structure of o-methylpsychotrine should be expressed by formula (III) with the endocyclic double bond. At the same time it is known that o-methylpsychotrine yields monoacyl derivatives in which the double bond can be only exocyclic. N-Benzoyl- and N-succinyl-o-methylpsychotrines, prepared from natural o-methylpsychotrine, have been described in the literature. We prepared N-acetyl derivatives of stereoisomeric o-methylpsychotrines by treatment of the ethereal solutions of the bases with acetic anhydride and aqueous alkali. The bases were isolated in an amorphous state but yielded crystalline oxalates. The melting points of the bases of N-acetyl-o-methylpsychotrines were close to the corresponding melting points of the bases of o-methylpsychotrine. However, the bases of N-acetyl-o-methylpsychotrine were more stable to the action of light, atmospheric oxygen and other external effects. If one dissolves the base of o-methylpsychotrine in carbon tetrachloride, the solution begins to cloud in a few minutes and a red precipitate forms; m. p. 171-178° (deforms at 164°). This resembles rubremetine chloride (m. p. 166-173°) in its appearance. A similar picture is not observed in a solution of N-acetyl-o-methylpsychotrine in carbon tetrachloride. The solution remains transparent for many days. The melting points of oxalates of N-acetyl-o-methylpsychotrines are also close to the corresponding melting points of oxalates of o-methylpsychotrines, but show a depression in mixed melting points with them. The ultraviolet spectra of bases of N-acetyl-o-methylpsychotrines (Fig. 5) and their oxalates (Fig. 6) turned out to be analogous to the corresponding spectra of o-methylpsychotrines. The same picture was observed in the case of 1-benzal-1,2,3,4-tetrahydro-2-methyl-6,7-methylenedioxyisoquinoline (XII). Therefore, the ultraviolet spectra are insufficiently dependable for the determination of the position of the double bond.
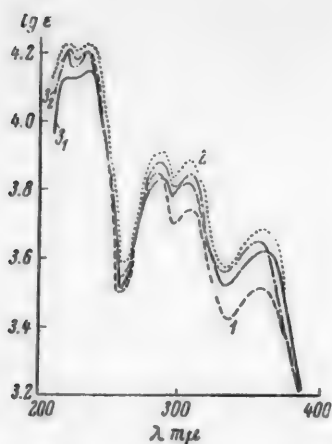


Fig. 2. Ultraviolet absorption spectra of oxalates of o-methylpsychotrines in ethyl alcohol. 1) Isomer 1; 2) isomer 2; 3) isomer 3.

Fig. 3. Ultraviolet absorption spectra of (+)-tartrates of o-methylpsychotrines in ethyl alcohol. 1) Isomer 1; 2) isomer 2; 3₁) isomer 3; 3₂) isomer 3 from mother liquor.

Infrared spectroscopy gives better results in many cases. In the case of o-methylpsychotrine the position of the double bond should succumb readily to a determination by means of infrared spectra since in the presence of an exocyclic double bond in the molecule, an NH group must be present and this has a definite, characteristic infrared absorption band at the region of 3500-3100 $cm^{-1}$ (2.86-3.23 $\mu$). The infrared spectrum of the base of o-methylpsychotrine, taken in vaseline oil, does not have any absorption bands at this frequency, which indicates the absence of an exocyclic double bond. The spectrum of the o-methylpsychotrine base in carbon tetrachloride also showed the absence of the NH group. We were obliged to omit taking the spectrum in a polyfluorocarbon, which is usually used for working in this region of the spectrum, since o-methylpsychotrine reacted instantly with this substance with formation of a red color. For comparison there was taken the spectrum of a standard substance — dihomoveratrylamine — at the same concentration. In this there was present the band of the NH group at 3293.5 $cm^{-1}$. The location of this band indicates that in this compound there is an intramolecular hydrogen bond.

Replacement of hydrogen by deuterium is often used in the study of the hydrogen bond, since this change is accompanied by a
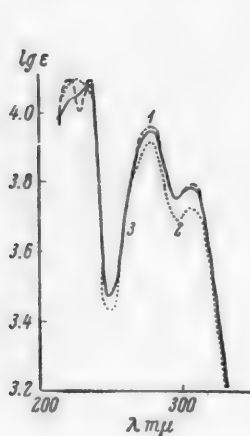


Fig. 4. Ultraviolet absorption spectra of bases of o-methylpsychotrine in ethyl alcohol. 1) Isomer 1; 2) isomer 2; 3) isomer 3.
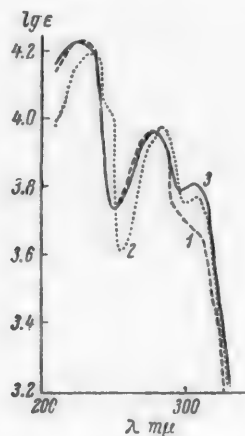


Fig. 5. Ultraviolet absorption spectra of bases of N-acetyl-o-methylpsychotrines in ethyl alcohol. 1) Isomer 1; 2) isomer 2; 3) isomer 3.
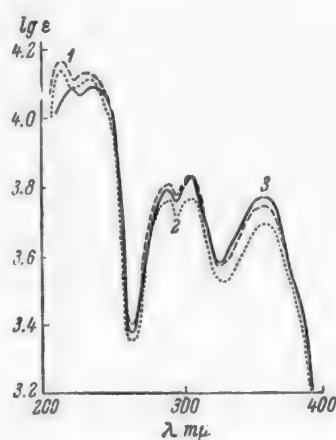


Fig. 6. Ultraviolet absorption spectra of oxalates of N-acetyl-o-methylpsychotrines in ethyl alcohol. 1) Isomer 1; 2) isomer 2; 3) isomer 3.

sharp displacement of the characteristic frequency to the side of longer wavelengths. We attempted to use this method of study in the hopes of locating the NH group in o-methylpsychotrine. It is known that deutero-hydrogen exchange in the alcohol and the amino groups occurs extraordinarily rapidly [11, 12], while the exchange of hydrogen bound to carbon either does not proceed at all or requires special conditions [13, 14]. The base of o-methylpsychotrine was dissolved in dry dioxane and treated with excess heavy water. After 2 days' standing the base was isolated and subjected to spectroscopic examination. The ND band also failed to be found, which indicates the absence of an exocyclic bond in o-methylpsychotrine. The deutero-hydrogen exchange failed to take place in the case of dihomoveratrylamine as well. This agrees with other known facts about the hindered hydrogen exchange at the hydrogen which participates in the formation of an intramolecular hydrogen bond. For example, hydrogen is not exchanged in 1-hydroxyanthraquinone [15] or 1-benzeneazo-2-naphthylamine [16]. In di-

homoveratrylamine, evidently, the oxygen of the methoxyl group, located in meta position in respect to the side chain (XIII), participates in the formation of the hydrogen bond.



(XII)          (XIII)
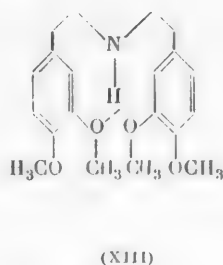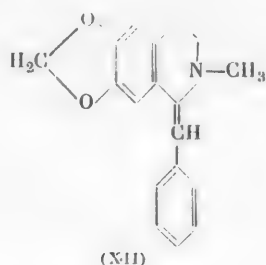
Thus, the infrared spectra of the base of o-methylpsychotrine confirm the presence in it of an endocyclic double bond. The spectroscopic study of salts of o-methylpsychotrine is extraordinarily complicated by the presence of water of crystallization in them. However, on the basis of the spectral data in the region of 1200-1700 cm$^{-1}$, it is possible to say sufficiently confidently that the salt is devoid of an NH group.

Summarizing all the above-said, we should consider that the structure of o-methylpsychotrine corresponds to formula (III). The formation of the mono-N-acyl derivatives may be explained by the presence of tautomerism between (II) and (III) with the predominant shift in the direction of the compound with endocyclic double bond (III). Such a shift of equilibrium in the direction of one of the possible forms is observed in neutral and acidic solutions of compounds capable of ketimide-enamine transformations. The exocyclic disposition of the double bond arises only under the action of alkali and is fixed by an acylating agent.

EXPERIMENTAL

I. β-(3",4"-Dimethoxyphenyl)-ethylamide of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (V). 1) From quinolizine prepared in cyclization with phosphorus oxychloride and hydrogenation of quinolizine chloride in the presence of platinum oxide in acid medium. Ethyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (IV) (0.72 g) and 1 g of homoveratrylamine were heated at 180-200° for 7 hrs in a nitrogen stream. 20 ml of dry ether was added to the reaction mixture after cooling and the whole was left overnight. Then, the solid amide was filtered off, washed with water on the filter to remove traces of homoveratrylamine, and dried in a desiccator. The yield was 0.6 g (60.2%). After recrystallization from ether, the amide formed a colorless crystalline substance, readily soluble in alcohol and chloroform, and difficultly in ether and petroleum ether, and insoluble in water; m. p. 144-145° (deforms slightly at 136.5°).

Found %: C 69.88; H 8.09; N 5.66, 5.68. C$_{29}$H$_{40}$O$_5$N$_2$. Calculated %: C 70.13; H 8.12; N 5.64.

2) From quinolizine prepared by cyclization of piperidone with phosphorus oxychloride and hydrogenation in the presence of platinum oxide in neutral medium. From 0.88 g of ethyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (IV) and 1 g of homoveratrylamine there was obtained 0.7 g (57.8%) of the amide, under the same conditions as in the previous experiment. The product was isolated from ether in the form of colorless crystals which were readily soluble in alcohol, chloroform and acetone, difficultly in ether, and petroleum ether, and insoluble in water. M. p. 147.5-148.5° (deforms at 145.5°).

Found %: C 70.06, 70.04; H 7.89, 7.92; N 5.75, 5.74. C$_{29}$H$_{40}$O$_5$N$_2$. Calculated %: C 70.13; H 8.12; N 5.64.

3) From quinolizine prepared by cyclization of piperidone with phosphorus oxychloride and hydrogenation in the presence of Raney nickel catalyst. From 3 g of methyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1,2:1',2')-quinolizyl-7-acetic acid (IV) and 3 g of homoveratrylamine, under the above-described conditions, there was obtained 2.6 g of the amide (60.5%). This separated in the form of colorless crystals from a mixture of anhydrous ethyl alcohol and petroleum ether (1:2). It was readily soluble in alcohol and chloroform, difficultly in benzene, toluene, ether and petroleum ether, and insoluble in water. M. p. 144-146.5° (deforms at 139°).

Found %: C 70.42, 70.25; H 8.37, 8.04; N 5.68, 5.76. $C_{29}H_{40}O_5N_2$. Calculated %: C 70.13; H 8.12; N 5.64.

II. o-Methylpsychotrine (III). From amide prepared from quinolizine isolated after hydrogenation in the presence of platinum oxide in acid medium. a) The base of o-methylpsychotrine. The amide (1.6 g), 15 ml of dry chloroform and 10 ml of phosphorus oxychloride were heated at gentle reflux for 4 hrs. The chloroform and excess phosphorus oxychloride were distilled off in vacuo. The residue was dissolved in 10 ml of 5% hydrochloric acid and extracted with 20 ml of ether to remove impurities. Then the cooled aqueous solution was made alkaline with ammonia. The separated base was extracted with ether, then with chloroform. The solvents were distilled off after drying with potassium carbonate. From the ethereal extract there was obtained 0.45 g of the base in the form of a slightly yellow oil, which rapidly solidified in vacuo, being transformed into a foam-like colorless amorphous substance. After removal of ether in vacuo, from a solution in dry ether of the residue obtained after evaporation of the solvent from the chloroform extract above, there was obtained an additional 0.5 g of the o-methylpsychotrine base. The yield was 0.95 g (61.6%). M. p. 59-60° (deforms at 52.5°).

b) Oxalate of o-methylpsychotrine was prepared by treatment of an ethereal solution of the base with an ethereal solution of oxalic acid. The oxalate attracts atmospheric moisture during filtration. After three recrystallizations from anhydrous methyl alcohol, the oxalate formed a colorless substance which was readily soluble in water, difficultly in alcohol and insoluble in ether. The substance was dried at 110° (1 mm) for 3 hrs prior to analysis for carbon and hydrogen. M. p. 147.5° (it deforms at 145.5-146.5°).

Found %: C 60.13; H 6.23; N 4.40. $C_{33}H_{42}N_2O_{12}$. Calculated %: C 60.17; H 6.43; N 4.25.

c) Base of o-methylpsychotrine was isolated from the oxalate. The 0.15 g of o-methylpsychotrine oxalate obtained above was dissolved in water and treated with ammonia. The separated base was extracted with ether and dried over anhydrous potassium carbonate. The base, after the distillation of ether, was isolated in the form of a colorless amorphous substance, readily soluble in organic solvents and insoluble in water. Yield was 0.1 g (79.5°). M. p. 59-60° (it deforms at 52.5°).

Found %: C 72.80; H 8.25; N 5.80. $C_{29}H_{38}O_4N_2$. Calculated %: C 72.77; H 8.00; N 5.85.

d) (+)-Tartrate of o-methylpsychotrine. To a solution of 0.2 g of the o-methylpsychotrine base in 2 ml of anhydrous ethyl alcohol there was added a solution of 0.15 g of (+)-tartaric acid in 4 ml of alcohol. A precipitate of (+)-tartrate precipitated immediately and was filtered off. The yield was 0.3 g (88%). The (+)-tartrate (0.3 g) was recrystallized from 5 ml of anhydrous ethyl alcohol. There was obtained 0.2 g of the product. After repeated recrystallization from 6 ml of alcohol, there was isolated 0.13 g of slightly yellowish substance, readily soluble in water, moderately in alcohol and acetone, and insoluble in ether. M. p. 125° (with decomposition) (deforms at 100°); $[\alpha]^{18}D$ +17.8° (c 3.4; water).

Found %: C 57.06; H 6.86; N 3.83, 3.86. $C_{29}H_{38}O_4N_2 \cdot 2C_4H_6O_6$. Calculated %: C 57.07; H 6.47; N 3.59.

2) From the amide prepared from quinolizine isolated after hydrogenation in the presence of platinum oxide in neutral medium. a) Base of o-methylpsychotrine. From 1.5 g of the amide there was obtained as a result of treatment analogous to that described above, 1.31 g (91%) of o-methylpsychotrine base in the form of a colorless amorphous substance. M. p. 50° (deforms at 40°).

b) The oxalate was prepared by the reaction of the base with oxalic acid in ethereal solution. The oxalate precipitate was filtered off and recrystallized 3 times from anhydrous methyl alcohol. The substance was dried at 110° (1 mm) for 3 hrs prior to analysis for carbon and hydrogen. M. p. 148° (decomp.) (deforms at 146.5°).

Found %: C 59.96, 60.21; H 6.57, 6.71; N 4.40, 4.22. $C_{33}H_{42}O_{12}N_2$. Calculated %: C 60.17; H 6.43; N 4.25.

c) o-Methylpsychotrine base isolated from the oxalate. From 0.15 g of the oxalate there was obtained 0.12 g (79.5%) of the base. M. p. 58-59° (deforms at 50°).

Found %: C 72.40; H 8.13; N 5.57. $C_{29}H_{38}O_4N_2$. Calculated %: C 72.77; H 8.00; N 5.85.

d) (+)-Tartrate of o-methylpsychotrine. The o-methylpsychotrine base (0.21 g) was dissolved in 3 ml of anhydrous ethyl alcohol and treated with 0.2 g of (+)-tartaric acid in 4 ml of alcohol. The precipitate of (+)-tartrate was recrystallized from 9 ml of anhydrous ethyl alcohol. There was obtained 0.1 g of product. After

repeated crystallization from 4.5 ml of alcohol there was isolated 50 mg of the product. (+)-Tartrate forms a slightly yellowish substance, readily soluble in water, moderately in alcohol and acetone and insoluble in ether. M. p. 125° (decomp.); $[\alpha]^{18}D$ +11.45° (c 4.66; water).

Found %: C 57.11; H 6.71; N 3.87, 3.60. $C_{29}H_{38}O_4N_2 \cdot 2C_4H_6O_6$. Calculated %: C 57.07; H 6.47; N 3.59.

3) From the amide prepared from quinolizine isolated after hydrogenation in the presence of Raney nickel catalyst. a) From 2.3 g of the amide there was obtained by the above-described method 2 g (91%) of the base in the form of colorless amorphous substance, readily soluble in alcohol and chloroform, difficultly in ether and insoluble in water. M. p. 60-61° (deforms at 38°).

b) o-Methylpsychotrine oxalate — a colorless crystalline substance, readily soluble in water, difficultly in alcohol and insoluble in ether. It was purified by three recrystallizations from anhydrous methyl alcohol. The substance was dried at 1 mm and 110° for 3 hrs prior to analysis. M. p. 147.5° (decomp.) (deforms at 145.5°).

Found %: C 60.31, 59.86; H 6.34, 6.41; N 4.40, 4.28. $C_{33}H_{42}O_{12}N_2$. Calculated %: C 60.17; H 6.43; N 4.25.

c) Base of o-methylpsychotrine isolated from the oxalate. From 0.15 g of the oxalate there was obtained 0.084 g (66.79%) of the base in the form of a colorless amorphous substance, readily soluble in alcohol and chloroform, difficultly in ether and insoluble in water. M. p. 58-59° (deforms at 50°).

Found %: C 72.53; H 8.32; N 5.77. $C_{28}H_{38}O_4N_2$. Calculated %: C 72.77; H 8.00; N 5.85.

d) (+)-Tartrate of o-methylpsychotrine. To 50 mg of the o-methylpsychotrine base in 2 ml of anhydrous ethyl alcohol there was added 31 mg of (+)-tartaric acid in 2 ml of alcohol. The resulting precipitate was filtered off. The yield was 40 mg (50%). M. p. 159° (decomp.) (deforms at 120°). It was recrystallized twice from a mixture of anhydrous ethyl alcohol and acetone. It was a nearly colorless substance with a slight pistachio shade, rather readily soluble in water and acetone, insoluble in ether. M. p. 160° (decomp.) (deforms at 123.5° slightly); $[\alpha]^{18}D$ +10.65° (c 3.98; water).

Found %: C 57.19; H 6.68; N 3.71. $C_{37}H_{50}O_{16}N_2$. Calculated %: C 57.07; H 6.47; N 3.59.

The alcoholic mother liquor, after the separation of the crystalline precipitate, was evaporated in vacuo. There was left a residue of 40 mg (50%); m. p. 120° (decomp.). It was recrystallized twice from a mixture of anhydrous alcohol and acetone. In its appearance and properties it duplicates the previously described tartrate. M. p. 160° (decomp.) (deforms at 120°); $[\alpha]^{18}D$ +16.1° (c 1.88; water).

Found %: C 57.13; H 6.62. $C_{37}H_{50}O_{16}N_2$. Calculated %: C 57.07; H 6.47.

III. N-Acetyl-o-methylpsychotrine. 1) From o-methylpsychotrine prepared from quinolizine isolated after hydrogenation in the presence of platinum oxide in acid medium. a) N-Acetyl-o-methylpsychotrine base. The base of o-methylpsychotrine (0.55 g) was dissolved in 50 ml of ether and treated with 7.7 ml of 10% aqueous solution of potassium hydroxide and 0.8 ml of acetic anhydride. The mixture was shaken in a separatory funnel for 10 min. The aqueous layer was separated and the ethereal layer was washed with a potassium hydroxide solution. The extract was dried with potassium carbonate. After distillation of ether, there was isolated the base of N-acetyl-o-methylpsychotrine in the form of a colorless amorphous powder. The yield was 0.52 g (86%); m. p. 78-79° (deforms at 40°).

Found %: C 71.87; H 7.57; N 5.47. $C_{31}H_{40}O_5N_2$. Calculated %: C 71.49; H 7.75; N 5.38.

b) N-Acetyl-o-methylpsychotrine oxalate. This was prepared by treatment of an ethereal solution of the base with an ethereal solution of oxalic acid. The oxalate attracts atmospheric moisture during filtration. It was recrystallized twice from anhydrous methyl alcohol. It was a colorless substance, readily soluble in water, difficultly in alcohol and insoluble in ether. M. p. 148.5° (decomp.) (deforms at 142°). The melting point of a mixture of the oxalate of N-acetyl-o-methylpsychotrine with the oxalate of o-methylpsychotrine was 141.5-148° (decomp.) (deforms at 137°).

Found %: C 57.74; H 7.1. $C_{31}H_{40}O_5N_2 \cdot C_2H_2O_4 \cdot 4H_2O$. Calculated %: C 58.04; H 7.38.

2) From o-methylpsychotrine prepared from quinolizine isolated after hydrogenation in the presence of platinum oxide in neutral medium. a) N-Acetyl-o-methylpsychotrine base. This was prepared as indicated in the previous experiment in nearly quantitative yield. M. p. 98-99° (deforms at 97°).

Found %: C 71.75; H 7.50; N 51.3. $C_{31}H_{40}O_5N_2$. Calculated %: C 71.49; H 7.75; N 5.38.

b) N-Acetyl-o-methylpsychotrine oxalate, m. p. 152° (decomp.) (deforms at 146°). The melting point of a mixture of the oxalate of N-acetyl-o-methylpsychotrine with the oxalate of o-methylpsychotrine was 142-150° (decomp.) (deforms at 138°).

Found %: C 58.35; H 7.15. $C_{31}H_{40}O_5N_2 \cdot C_2H_2O_4 \cdot 4H_2O$. Calculated %: C 58.04; H 7.38.

3) From o-methylpsychotrine prepared from quinolizine isolated after hydrogenation in the presence of Raney nickel catalyst. a) N-Acetyl-o-methylpsychotrine base, m. p. 73-74° (deforms at 40°).

b) N-Acetyl-o-methylpsychotrine oxalate, m. p. 151° (decomp.) (deforms slightly at 143.5°). The melting point of a mixture of the oxalate of N-acetyl-o-methylpsychotrine and the corresponding oxalate of o-methylpsychotrine was 142.5-50° (deforms at 138.5°).

Found %: C 58.35; H 7.15. $C_{31}H_{40}O_5N_2 \cdot C_2H_2O_4 \cdot 4H_2O$. Calculated %: C 58.04; H 7.38.

## SUMMARY

1. The synthesis of isomeric o-methylpsychotrines was accomplished.

2. The studies made on o-methylpsychotrine and its acyl derivatives permit us to conclude that the bases and the salts of the alkaloids have predominantly endocyclic $N = C$ position of the double bond. In the alkaline medium there occurs a migration of hydrogen (prototropic rearrangement) with formation of an exocyclic $C = C$ bond.

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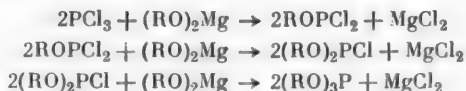# FROM THE FIELD OF ORGANIC INSECTOFUNGICIDES

## XXXIV. NEW METHOD OF SYNTHESIS OF TRIALKYL PHOSPHITES

N. N. Mel'nikov, Ia. A. Mandel'baum and Z. M. Bakanova

Various derivatives of phosphonic acids, such as, for example, the derivatives of phosphonoacetic acid, used for control of plant pests [1, 2] have received a practical application in agriculture as chemical means of protection of plants in recent years, along with the esters of phosphoric, thiophosphoric and dithiophosphoric acids. The basic raw material for the preparation of compounds of this type are the trialkyl phosphites which are beginning to acquire an independent significance in agriculture as the means for control of weeds [3]. In connection with this information we undertook a special study of the methods of preparation of trialkyl phosphites.

At the present time there have been described in the literature four methods of synthesis of trialkyl phosphites: 1) the method of A. E. Arbuzov, by the reaction of phosphorus trichloride with sodium alcoholates in ether or another suitable solvent [4, 5]; 2) the method of Milobendzki , by the reaction of phosphorus trichloride with alcohols in the presence of organic bases [6-8]; 3) the reaction of transesterification [14] and 4) from sodium salts of acid esters of carbonic acid and phosphorus trichloride [15]. Among the listed methods of preparation of trialkyl phosphites, the most practical interest, in our opinion, lies in the first two methods. However, in the second method one obtains a not very pure product, while in the first, one is obliged to work with metallic sodium which is inconvenient in some cases, while the yields at times do not rise over 20-30%.

Analogous to the method of preparation of esters of chlorothiophosphoric acid developed by us recently [16-18], we used for the preparation of trialkyl phosphites the reaction of phosphorus trichloride with magnesium alcoholates which are readily prepared from the corresponding alcohol and metallic magnesium.

$$2PCl_3 + (RO)_2Mg \rightarrow 2ROPCl_2 + MgCl_2$$
$$2ROPCl_2 + (RO)_2Mg \rightarrow 2(RO)_2PCl + MgCl_2$$
$$2(RO)_2PCl + (RO)_2Mg \rightarrow 2(RO)_3P + MgCl_2$$

As intermediate products there are formed the esters of chlorophosphorous acid, which under appropriate conditions may be isolated readily. The trialkyl phosphites may be obtained in 35-60% yields from this reaction. The compounds prepared by us and their properties are listed in the table.

## EXPERIMENTAL

Preparation of trialkyl phosphites. As an example, we describe the preparation of triethyl phosphite by two methods.

1. To magnesium ethoxide prepared from 5.5 g of metallic magnesium (powder) and 27 ml of anhydrous ethyl alcohol in 75 ml of dry ether there was added over 30 min with good stirring 13.7 g of phosphorus trichloride. The temperature of the reaction mixture rose from 20° to the boiling point of ether during the addition of phosphorus trichloride. After addition of the entire amount of phosphorus trichloride, the reaction mixture was refluxed on a water bath for 1.5 hr. Then, after cooling, the precipitated magnesium chloride was filtered off, ether was distilled and the residue distilled in vacuo or at atmospheric pressure. B. p. 154-155°. Yield: 9-10 g (56-60%).

Properties of Trialkyl Phosphites

| Formula | Yield (in %) | $d_4^{20}$ | $n_D^{20}$ | B. p. (pressure in mm) | M R | | P (in %) | | C (in %) | | H (in %) | | Literature data [19, 20] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | found | calc. | found | calc. | found | calc. | found | calc. | b. p. (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ |
| $(C_2H_5O)_3P$ | 55—60 | 0.9665 | 1.4136 | 151—155° | 42.75 | 42.97 | 18.50, 18.65 | 18.68 | — | — | — | — | 155—156° [10] | 0.9777(0°) | 1.4138 |
| $(C_3H_7O)_3P$ | 41 | 0.9525 | 1.4290 | 83 (10) | 56.41 | 56.82 | 14.58, 14.50 | 14.90 | 51.87, 52.06 | 51.90 | 10.17, 10.12 | 10.10 | 83 (10) [19] | 0.9522 | 1.4265 |
| $(C_4H_9O)_3P$ | 35 | 0.9267 | 1.4320 | 137 (26) | 70.28 | 70.67 | 12.45, 12.51 | 12.40 | 57.41, 57.52 | 57.60 | 10.80, 10.81 | 10.80 | 127 (18) [20] | 0.9253 | 1.4321 |
| iso-$(C_4H_9O)_3P$ | 60 | 0.9060 | 1.4330 | 112 (14) | 70.71 | 70.67 | 12.41, 12.46 | 12.40 | 57.30, 57.26 | 57.60 | 10.91, 10.86 | 10.80 | 135—136 (10) [19] | 0.9036 | — |

• In Russian.

2. To dry powdered magnesium ethoxide suspended in 75 ml of absolute ether there was gradually added 13.7 g of phosphorus trichloride and the reaction mixture was worked up further as described above. Magnesium ethoxide was prepared by the dissolution of 5.5 g of metallic magnesium in 70 ml of anhydrous alcohol with a subsequent distillation of excess alcohol in vacuo from a water bath. The yield of triethyl phosphite by this method was 55%.

Under completely analogous conditions there were prepared the other trialkyl phosphites, except trimethyl phosphite, the yield of which was poor. It is possible to use benzene or petroleum ether as the solvent instead of ether, but the yields of trialkyl phosphites in these cases are lower.

## SUMMARY

A new method of preparation of trialkyl phosphites in yields of 35-60% by the reaction of phosphorus trichloride with magnesium alcoholates has been developed and proposed.

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# CATALYTIC SYNTHESIS OF KETONES

## V. SYNTHESIS OF METHYL PHENYL, ETHYL PHENYL, METHYL n-PROPYL, AND DI-n-PROPYL KETONES

I. P. Iakovlev and D. P. Popa

One of us had previously made a supposition [1] that alcohols which cannot be dehydrated to ethylenic compounds should not form ketones and proposed a general scheme of ketonization [2]. In the present work the above supposition was verified experimentally and some theories were developed about the mechanism of ketonization in which two carbonyl-containing compounds take part in the reaction. We studied the following mixtures: 1) benzoic acid and ethyl alcohol, 2) acetic acid and benzyl alcohol, 3) benzoic acid and methyl alcohol, 4) benzaldehyde and acetic acid, 5) n-butyraldehyde, 6) n-butyraldehyde and acetic acid, and 7) ethyl benzoate and ethyl alcohol. Benzoic acid and methyl alcohol, and acetic acid and benzyl alcohol, as indicated earlier [1], should not form either acetophenone or methyl benzyl ketone, while benzoic acid and ethyl alcohol should yield ethyl phenyl ketone. The synthesis of methyl ethyl ketone from acetic acid and ethyl alcohol had been carried out earlier [3]. The reaction was run on chrome-manganese catalyst [8].

Actually, as shown by our experiments, neither acetophenone was formed from benzoic acid and methyl alcohol, nor was methyl benzyl ketone formed from acetic acid and benzyl alcohol, as expected, while ethyl phenyl ketone did form from benzoic acid and ethyl alcohol. It should be noted that in the reaction of acetic acid and benzyl alcohol there was observed the formation of acetophenone. This reaction does not fit either our schemes of ketonization reactions or the schemes according to which the formation of ketones proceeds either through esters or through aldols [4-7]. We supposed that the formation of acetophenone from acetic acid and benzyl alcohol proceeds analogously to the reaction of ketonization of acetic and benzoic acids. Benzyl alcohol is transformed by dehydrogenation at first into benzaldehyde, after which the resulting benzaldehyde reacts with acetic acid. This supposition is confirmed by the fact that in the reaction of acetic acid and benzaldehyde there is formed some acetophenone. This reaction showed that acetophenone is evidently formed in the reaction of acetic acid and benzaldehyde, but not benzyl alcohol, and that it is a special case of a general scheme of ketonization of compounds with carbonyl groups [2]. If this is correct, n-butyraldehyde should yield di-n-propyl ketone. The mixture of n-butyraldehyde and acetic acid should yield methyl propyl ketone, along with acetone and di-n-propyl ketone. Actually, during ketonization of a mixture of acetic acid with n-butyraldehyde there were obtained the expected ketones — acetone, methyl propyl ketone and di-n-propyl ketone.

The general scheme of ketonization of compounds which have carbonyl groups, proposed by us, permits one to forecast the direction of the ketonization processes. It would be possible, for example, to say that on the dehydrogenating catalysts, such as copper, there would be formed mainly acetone from a mixture of acetic acid and ethyl alcohol, while over a dehydrating catalyst, for example, aluminum oxide, methyl ethyl ketone would be formed.

## EXPERIMENTAL

1. Experiments with benzoic acid and ethyl alcohol. A solution of ethanol saturated at room temperature with benzoic acid was fed from an automatic burette into the catalyst tube made of Pyrex glass, the feed rate being 15 ml per hour. The chrome-manganese catalyst [8] was deposited on asbestos wool.

For determination of optimum reaction conditions, the reaction was run at 440, 450 and 460°. In all experiments hydrogen was supplied to the system at the rate of 75 ml per min. The hydrogen was obtained from arsenic-

| Composition of the starting mixture | Amount (ml) | | b. p. and amount of main fraction (in g) | Low boiling fraction and its amount (in g) | Melting point | | | Name of ketone | Yield of ketone (in %) | Constants of main fraction | | | | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | of mixture run through | of catalyzate | | | of 2,4-dinitro-phenylhydrazone of ketone of main fraction | of 2,4-dinitro-phenylhydrazone of ketone [9] | of semicarbazone of ketone of main fraction | | | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ found | $MR_D$ calculated | |
| Benzoic acid + ethyl alcohol [a] | 150 | 58 | 215—220° (2.6) | 170—215° (4.8) | 189—192° | 191° | 178° | Ethyl phenyl ketone | 7 [c] | 1.020 | 1.525 | 40.32 | 40.17 | Fraction with b. p. 170—215° consisted mainly of benzaldehyde |
| Ethyl benzoate + ethyl alcohol (0.28:2) [b] | 147 | 28 | 216—223 (3.7) | 200—208 (6.6) | 190—192 | 191 | | Ethyl phenyl ketone | 7.8 [e] | — | — | — | — | Experiment was run with $H_2$ gas |
| Benzyl alcohol + acetic acid (1:1) [b] | 65 | 53 | 190—202 (2.0) | | 242—243 | 249 | 197 | Acetophenone | | — | — | — | — | Experiments were run with $H_2$ and without $H_2$. Besides acetophenone, there were isolated: acetone, toluene, benzaldehyde |
| Benzaldehyde + acetic acid (1:4) [b] | 55 | 44 | 196—205 (2.1) | 189—196 (0.7) | 240—242 | 249 | 197—198 | Acetophenone | 13 [d] | 1.030 | 1.538 | 36.44 | 35.55 | Feed rate 12 ml per hr |
| Benzoic acid + methyl alcohol [a] | 50 | 36 | 176—187 (11.5) | | 236 | 237 | 226 | Benzaldehyde | | 1.045 | 1.540 | 31.86 | 30.93 | Experiments were run with $H_2$ and without it |
| n-Butyraldehyde | 55 | 21.5 | 142—148 (9.1) | | 73—74 | 75 | | Di-n-propyl ketone | 41 | 0.821 | 1.406 | 34.16 | 34.53 | Experiments were run with $H_2$ at 440° |
| Acetic acid + n-butyraldehyde (4.5:1) [b] | 190 | 91 { | 140—148 (6.6) | | 74 | 75 | | Di-n-propyl ketone | 35.5 [d] | 0.8213 | 1.406 | 34.00 | 34.53 | Experiments were run without $H_2$ |
| | | | 99—105 (8.1) | | 142 | 143 | | Methyl-n-propyl ketone | 28.8 [d] | 0.8095 | 1.388 | 25.20 | 26.11 | |

a) Saturated solution at room temperature;  b) molar ratio;  c) calculated on the acid;  d) calculated on the aldehyde;  e) calculated on the ester.

free zinc and dilute sulfuric acid. The catalyzate, after being dried, was subjected to fractional distillation. The results of this and subsequent experiments are shown in the table. The optimum reaction temperature was found to be 450° and the experiments were run at this level.

Fractions with b. p. 170-251° consisted mainly of benzaldehyde and a small amount of acetophenone. A few drops of the fraction were taken at the beginning and the end of distillation for preparation of derivatives with 2,4-dinitrophenylhydrazine. The tests of the resulting 2,4-dinitrophenylhydrazones of acetone and benzaldehyde in mixed melting points with authentic compounds gave respective m. p. 234° and 243°. The fraction with b. p. 215-220° was ethyl phenyl ketone (b. p. 218°). Ethyl phenyl ketone was characterized by the melting points of its 2,4-dinitrophenylhydrazone and semicarbazone.

2. Experiments with ethyl benzoate and ethyl alcohol were run at 450° over chrome-manganese catalyst (15 g) deposited on asbestos wool. The feed rate of the initial mixture was 50 ml/hr; hydrogen was supplied at the rate of 100 ml/min. Two layers formed — aqueous and oily. The latter was separated and dried over sodium sulfate. After distillation there were isolated: acetone, acetophenone and ethyl phenyl ketone. The yield of ethyl phenyl ketone, as in the previous experiment, was negligible.

3. Experiments with benzyl alcohol and acetic acid, were run under conditions analogous to those described for the 1st experiment. Acetophenone was characterized by the melting point of its derivatives, whose mixed melting points gave no depression. It was impossible to fractionate the mixture into the various components in this experiment. As follows from our scheme, evolution of carbon monoxide should occur in the formation of acetophenone from acetic acid and benzyl alcohol. Actually, the gas analysis run in the VTI apparatus confirmed our expectations. In the off-gases there were found 38% of carbon monoxide and 1.5% carbon dioxide; unsaturated hydrocarbons were absent, while hydrogen was not determined.

4. Experiments with benzaldehyde and acetic acid. For confirmation of the fact that acetophenone is formed from benzyl alcohol and acetic acid through benzaldehyde, there was run an experiment with these substances. The results were similar to those from the preceding experiment (see Table).

5. Experiments with methyl alcohol and benzoic acid were run analogously with those described in Expt. 1. Methanol and benzaldehyde were detected in the examination of the resulting catalyzate. No acetophenone was found.

6. Experiments with n-butyraldehyde and its mixture with acetic acid were run under conditions analogous to those described in Expt. 1.

## SUMMARY

The reaction of ketonization of acids and aldehydes over a chrome-manganese catalyst was studied. From a mixture of acetic acid and benzyl alcohol it was impossible to isolate any methyl benzyl ketone. No acetophenone was formed from benzoic acid and methanol. Benzoic acid and ethyl benzoate form ethyl phenyl ketone with ethanol. n-Butyraldehyde with acetic acid gave methyl n-propyl ketone and di-n-propyl ketone. Benzaldehyde and acetic acid gave acetophenone.

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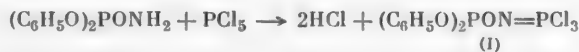
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# REACTION OF PHOSPHORUS PENTACHLORIDE WITH AMIDES
## OF PHOSPHORIC ACID

### A. V. Kirsanov and I. N. Zhmurova

In the reaction of phosphorus pentachloride with aryl- and alkylsulfonamides [1], amides of carboxylic acids [2] and amides of carbonic acid [3] there are formed the corresponding trichlorophosphazo compounds. This allows one to suppose that this reaction has a general character and could be extended to amides of other acids, including phosphoric and thiophosphoric. In reality, diphenyl phosphoramidate and diphenyl thiophosphoramidate react with phosphorus pentachloride yielding thereby the diphenyl esters of trichlorophosphazophosphoric and trichlorophosphazothionophosphoric acids.

$$(C_6H_5O)_2PONH_2 + PCl_5 \longrightarrow 2HCl + (C_6H_5O)_2PON{=}PCl_3$$
$$(I)$$
$$(C_6H_5O)_2PSNH_2 + PCl_5 \longrightarrow 2HCl + (C_6H_5O)_2PSN{=}PCl_3$$
$$(II)$$

The reaction proceeds in almost quantitative yield at room temperature.

Trichlorophosphazo compounds (I) and (II) are colorless viscous liquids which are readily soluble in benzene, carbon tetrachloride and dioxane, insoluble in petroleum ether. They are slowly hydrolyzed by water and atmospheric moisture.

Diphenyl ester of trichlorophosphazophosphoric acid forms the diphenyl ester of trianilinophosphazophosphoric acid, $(C_6H_5O)_2PON{=}P(NHC_6H_5)_3$, on being heated with aniline in a benzene solution. The diphenyl ester of trichlorophosphazothionophosphoric acid forms, in its reaction with aniline, a viscous extensible mass from which we failed to isolate any individual substances.

In the hydrolysis of substances (I) and (II) with formic acid there are formed the corresponding dichlorides: $(C_6H_5O)_2PONHPOCl_2$ (III) and $(C_6H_5O)_2PSNHPOCl_2$ (IV). The dichloride (III) is a viscous liquid which is soluble in benzene, carbon tetrachloride and dioxane, insoluble in petroleum ether. The dichloride (IV) is a colorless crystalline substance, readily soluble in dioxane, less soluble in benzene and carbon tetrachloride and insoluble in petroleum ether. Dichlorides (III) and (IV) react with aniline, yielding, respectively, the P,P-dianilide of P',P'-diphenyl ester of imidodiphosphoric acid and P,P-dianilide of P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid: $(C_6H_5O)_2PONHPO(NHC_6H_5)_2$ and $(C_6H_5O)_2PSNHPO(NHC_6H_5)_2$; colorless crystalline substances which have acidic character. They are titrated by one equivalent of alkali in an alcoholic solution.

In the reaction of diphenyl ester of trichlorophosphazophosphoric acid (I) with water there is formed, in good yield, the P,P-diphenyl ester of imidodiphosphoric acid, $(C_6H_5O)_2PONHPO(OH)_2$ (V). The hydrolysis with hot water requires a few minutes, while at room temperature the reaction is completed in 1 day. Substance (V) forms colorless crystals soluble in alcohol and dioxane, very difficultly soluble in water, and insoluble in benzene, ether or petroleum ether. The extraordinary stability of the N—P bond in substance (V) attracts attention. The aryl- and alkylsulfonamidophosphoric and acylamidophosphoric acids, analogous to it, are hydrolyzed comparatively readily by water yielding the corresponding amides [4], while the diphenyl ester of imidodiphosphoric acid is not decomposed by being boiled with water for 5-10 min. Aryl- and alkylsulfonamidophosphoric acids and acylamidophosphoric acids are readily soluble in cold water [4], but substance (V) is very difficultly soluble in water. Such

unusual properties of the P,P-diphenyl ester of imidodiphosphoric acid are caused, in all probability, by the presence of an intramolecular hydrogen bond:

$$
\begin{array}{c}
\text{H} \\
\text{O} \cdots \text{O} \\
\text{C}_6\text{H}_5\text{O} \diagdown \underset{\parallel}{\text{P}} \diagup \diagdown \underset{\parallel}{\text{P}} \diagup \text{OH} \\
\text{C}_6\text{H}_5\text{O} \diagup \quad \text{N} \quad \diagdown \text{O} \\
\text{H} \qquad \text{(V)}
\end{array}
$$
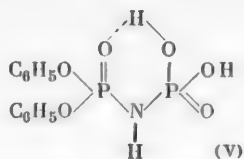
As is known, the sulfur atom is not inclined to form a hydrogen bond. Therefore, the diphenyl ester of trichlorophosphazothionophosphoric acid (II) is slowly decomposed in its reaction with water, yielding diphenyl thionophosphoramidate and phosphoric acid, without forming a sulfur analog of (V).

Diphenyl esters of trichlorophosphazophosphoric (I) and thionophosphoric (II) acids yield, in reactions with sodium aryloxides, the triaryloxy phosphazo compounds of types: $(C_6H_5O)_2PON=P(OR)_3$ (VI) and $(C_6H_5O)_2PSN=P(OR)_3$ (VII), which form colorless crystalline substances of neutral character.

Dichlorides (III) and (IV) react with alcoholates and phenolates forming tetra esters of the types: $(C_6H_5O)_2 \cdot PONHPO(OR)_2$ (VIII) and $(C_6H_5O)_2PSNHPO(OR)_2$ (IX). Tetraphenyl esters of types (VIII) and (IX) were also prepared by hydrolysis of diphenyl esters of triphenoxyphosphazophosphoric acids of types (VI) and (VII) according to the scheme:

$$(C_6H_5O)_2PON=P(OC_6H_5)_3 \xrightarrow{+2NaOH} C_6H_5ONa + H_2O + (C_6H_5O)_2PONNaPO(OC_6H_5)_2$$

For running this reaction it is unnecessary to isolate the appropriate triphenoxy phosphazo compound in the pure form and one may start directly with the crude reaction products of diphenyl esters of trichlorophosphazophosphoric and trichlorophosphazothionophosphoric acids with sodium phenoxide (see experimental section).

Di-p-nitrotetraphenyl esters of types (VIII) and (IX) are subject to a very rapid further hydrolysis on being heated with alkali. Therefore, in the hydrolysis of diphenyl ester of tri-p-nitrophenoxyphosphazophosphoric acid (VI, $R = C_6H_4NO_2$-p) with caustic alkali it is impossible to isolate the corresponding dinitrotetraphenyl ester, while after a brief heating with alkali of the diphenyl ester of tri-p-nitrophenoxyphosphazothionophosphoric acid (VII, $R = C_5H_4NO_2$-p) it was possible to isolate the dinitrotetraphenyl ester in a yield of but 12%. The diphenyl esters of triaryloxyphosphazophosphoric acids are not hydrolyzed by solutions of caustic alkalies at room temperature or by soda solutions at the boiling point.

P,P-Di-p-nitrotetraphenyl ester of P'-thionoimidodiphosphoric acid was prepared in 22% yield from the P,P-dichloride of P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid (IV) and sodium p-nitrophenoxide. From the P,P-dichloride of P',P'-diphenyl ester of imidodiphosphoric acid (III) and sodium p-nitrophenoxide we could not prepare the corresponding tetra ester.

Tetraaryl esters of imidodiphosphoric and thionoimidodiphosphoric acids of types (VIII) and (IX) are colorless crystalline compounds with acid character. They are titrated by one equivalent of alkali in an alcoholic solution.

## EXPERIMENTAL

Diphenyl ester of trichlorophosphazophosphoric acid (I). A mixture of 0.1 mole of diphenyl phosphoramidate and 0.1 mole of phosphorus pentachloride was allowed to stand at room temperature. Evolution of hydrogen chloride began soon and the mixture liquefied gradually. After 5-6 hrs the reaction mixture was heated for 30 min to 50-60°. The resulting diphenyl ester of trichlorophosphazophosphoric acid was a colorless viscous liquid; yield: 99.4%.

Found %: Cl 27.70. Equivalents after hydrolysis 4.97. $C_{12}H_{10}O_3NCl_3P_2$. Calculated %: Cl 27.78. Equivalents after hydrolysis 5.00.

Diphenyl ester of trichlorophosphazothionophosphoric acid (II) was prepared analogously to the preceding compound. It was a colorless viscous liquid; yield: 99.5%.

Found: equivalents after hydrolysis 4.86. $C_{12}H_{10}O_2NCl_3P_2S$. Calculated: equivalents after hydrolysis 5.00.

Diphenyl ester of trianilinophosphazophosphoric acid. A mixture of 0.01 mole of (I), 10 ml of benzene and 0.06 mole of aniline was refluxed for 5 hrs. After cooling, the resulting precipitate was filtered off and washed with benzene and with water to remove aniline hydrochloride. The water-insoluble diphenyl ester of trianilino-phosphazophosphoric acid was recrystallized from alcohol; colorless plates; yield: 76%; m. p. 195-197°.

Found %: N 10.33. $C_{30}H_{28}O_3N_4P_2$. Calculated %: N 10.01.

P,P-Dichloride of P',P'-diphenyl ester of imidodiphosphoric acid (III). A mixture of 0.1 mole of (I) and 0.1 mole of anhydrous formic acid was heated to 90-100°, then to 120-125° until gas evolution ceased (about 1.5-2 hrs). The resulting dichloride was a colorless, very viscous liquid; yield: 99.5%.

Found: equivalents after hydrolysis 3.91. $C_{12}H_{11}O_4NCl_2P_2$. Calculated: equivalents after hydrolysis 4.00.

P,P-Dichloride of P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid (IV). A mixture of 0.1 mole of (II), 0.1 mole of anhydrous formic acid and 10 ml of dry benzene was heated to 30-35° for 3 days until the gas bubbles ceased to be formed. 20 ml of petroleum ether was added to the reaction mixture and the resulting precipitate was filtered off and recrystallized from carbon tetrachloride. Yield: 30%. Colorless needles with m. p. 102-104°.

Found %: Cl 18.73. Equivalents after hydrolysis 4.06. $C_{12}H_{11}O_3NCl_2SP_2$. Calculated %: Cl 18.64. Equivalents after hydrolysis 4.00.

P,P-Dianilide of P',P'-diphenyl ester of imidodiphosphoric acid. A mixture of 0.01 mole of (III), 10 ml of benzene and 0.04 mole of aniline was refluxed for 5 hrs. The resulting precipitate was filtered off and washed with benzene, then with water to remove aniline hydrochloride. The water-insoluble dianilide was recrystallized from methanol. Colorless needles; yield: 54%; m. p. 197-198°.

Found %: N 9.02. Equivalents 1.00. $C_{24}H_{23}O_4N_3P_2$. Calculated %: N 8.77. Equivalents 1.00.

P,P-Dianilide of P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid was prepared from substance (IV) analogously to the preceding one; yield 98%; m. p. 198-200° (from alcohol).

Found %: N 8.68. $C_{24}H_{23}O_3N_3P_2S$. Calculated %: N 8.48.

P,P-Diphenyl ester of imidodiphosphoric acid (V). To 0.01 mole of (I) there was added 5 ml of water and the mixture was left overnight. The precipitated crystals of (V) were filtered off, washed with water, dried in air, dissolved in dioxane and precipitated with ether. It formed a colorless crystalline powder; m. p. 170-172°; yield: 83%.

Found %: N 4.43. Equivalents 2.09. M (in dioxane) 340, 348. $C_{12}H_{13}O_6NP_2$. Calculated %: N 4.25. Equivalents 2.00. M 329.

Diphenyl ester of triphenoxyphosphazophosphoric acid (VI, R = $C_6H_5$). To a solution of 0.02 mole of (I) in 25 ml of benzene there was added in one portion with energetic stirring 0.06 mole of sodium phenoxide. The mixture warmed up rather considerably owing to the heat of reaction and the sodium phenoxide passed into solution while a slimy precipitate of sodium chloride formed. After the heat evolution had ceased, the mixture was refluxed for 1 hr. After cooling, the sodium chloride was washed off with water, the benzene layer was separated, benzene was removed from it on a water bath and the residual oil was triturated with water until it crystallized. The crystalline product was filtered off, dried in air and recrystallized from a mixture of benzene and petroleum ether. Yield: 76% needles with m. p. 72-74°.

Found %: N 2.56. $C_{30}H_{25}O_6NP_2$. Calculated %: N 2.51.

Diphenyl ester of triphenoxyphosphazothionophosphoric acid (VII, R = $C_6H_5$) was prepared analogously to the preceding one. The crude specimen was washed with methanol and recrystallized from methanol. Prisms with m. p. 96-98°. Yield: 69%.

Found %: N 2.62. $C_{30}H_{25}O_5NSP_2$. Calculated %: N 2.44.

Diphenyl ester of tri-p-nitrophenoxyphosphazophosphoric acid (VI, R = $C_6H_4NO_2$-p). A mixture of 0.01 mole of (I), 0.03 moles of anhydrous sodium p-nitrophenoxide and 15 ml of dioxane was refluxed until the nitrophenoxide color faded out (about 2 hrs), after which it was poured into water. The resulting oil crystallized rapidly and the crystals were filtered off, washed with methanol and recrystallized from benzene. Yield: 78%. M. p. 132-134°.

Found %: N 8.30. $C_{30}H_{22}O_{12}N_4P_2$. Calculated %: N 8.09.

Diphenyl ester of tri-p-nitrophenoxyphosphazothionophosphoric acid (VII, R = $C_6H_4NO_2$-p) was prepared analogously to the preceding compound. Yield: 70%. M. p. 154-156°; prisms from benzene.

Found %: N 7.90. $C_{30}H_{22}O_{11}N_4SP_2$. Calculated %: N 7.90.

Diphenyl ester of tri-p-chlorophenoxyphosphazothionophosphoric acid (VII, R = $C_6H_4Cl$-p). 0.06 g-mole of p-chlorophenol was added to a solution of sodium methoxide prepared from 0.06 g-atom of sodium and 20 ml of methanol. The methanol was distilled in vacuo and to the solid phenoxide was added 25 ml of benzene and 0.02 mole of (I). The mixture was heated to boiling for 1.5 hrs, the precipitated sodium chloride was washed away with water, the benzene layer was separated, the benzene was distilled from it and the residual oil was triturated with methanol, after which it crystallized. The crystals were filtered off and recrystallized from methanol. Prisms with m. p. 69-71°. Yield: 36%.

Found %: Cl 15.79. $C_{30}H_{22}O_5NCl_3P_2$. Calculated %: Cl 15.74.

P,P-Dimethyl P',P'-diphenyl ester of imidodiphosphoric acid (VIII, R = $CH_3$). A solution of 0.06 mole of sodium methoxide in 20 ml of methanol was slowly added with stirring and cooling with ice water to a solution of 0.02 mole of (III) in 25 ml of benzene. The solvents were distilled off in vacuo on a water bath and the sirupy residue (a mixture of sodium chloride and the sodium salt of the tetra ester) was dissolved in 10 ml of water. The solution was acidified with hydrochloric acid and the precipitated oil (free tetra ester) was extracted with chloroform; chloroform was distilled off, the oily residue was dissolved in methanol, the solution was boiled with activated charcoal, filtered and the methanol was distilled off in vacuo. The residue was the tetra ester in the form of a viscous slightly yellowish oil; yield: 90%.

Found %: N 3.90. Equivalents 1.00. $C_{14}H_{17}O_6NP_2$. Calculated %: N 3.90. Equivalents 1.00.

P,P-Diethyl P',P'-diphenyl ester of imidodiphosphoric acid (VIII = $C_6H_5$) was prepared just like the preceding compound but, after the acidification of the aqueous solution of the salt, the free tetra ester was extracted with ether. The further work-up was as above. The tetra ester was a slightly yellowish viscous oil. Yield: 93%.

Found %: N 3.63. Equivalents 1.00. $C_{16}H_{21}O_6NP_2$. Calculated %: N 3.64. Equivalents 1.00.

Tetraphenyl ester of imidodiphosphoric acid (VIII, R = $C_6H_5$). A. From P,P-dichloride of P',P'-diphenyl ester of imidodiphosphoric acid. To a mixture of 0.06 mole of sodium phenoxide and 25 ml of benzene there was added, with energetic stirring, a solution of 0.02 mole (III) in 10 ml of benzene. After the vigorous reaction had been completed, the mixture was refluxed for 1 hr, after which benzene was distilled off in vacuo; the residue was treated with 25 ml of water and with enough hydrochloric acid to give an acid test with Congo red. The precipitated oil was separated from the aqueous layer by decantation and was rubbed with 50% methanol. The resulting crystalline precipitate was filtered off and recrystallized from a mixture of benzene and petroleum ether. Yield: 13%. Needles, m. p. 110-112°.

Found %: N 3.11. Equivalents 1.01. $C_{24}H_{21}O_6NP_2$. Calculated %: N 2.91. Equivalents 1.00.

B) From diphenyl ester of trichlorophosphazophosphoric acid. A solution of 0.02 mole of (I) in 10 ml of benzene was added to a suspension of sodium phenoxide in 25 ml of benzene. The reaction proceeded with heat evolution. After the heat evolution had ceased, the mixture was refluxed for 1 hr, after which it was washed with water, the benzene layer was separated and the benzene was distilled in vacuo. To the residue there was added 20 ml of methanol and 20 ml of N solution of sodium hydroxide. The mixture was refluxed for 30 min, poured into water and acidified. The tetraphenyl ester of imidodiphosphoric acid, which precipitated as an oil, crystallized rapidly. The crystals were filtered off, treated with a small volume of methanol to remove the colored impurities and recrystallized from a mixture of benzene and petroleum ether. Yield: 57%. The tetra ester melted at 110-112° and gave no depression in mixed melting point with the substance prepared in the preceding experiment.

P,P-Dimethyl P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid (IX, R = CH$_3$). To a mixture of 0.02 mole of (IV) and 20 ml of benzene there was added, with ice water cooling and energetic stirring, a solution of 0.06 mole of sodium methoxide in 20 ml of methanol, the addition being made gradually. The solvents were distilled in vacuo, the residual thick sirup was dissolved in water and the solution was acidified. An oil precipitated and soon crystallized. The crystals were filtered off and recrystallized from a mixture of benzene and petroleum ether. Prisms with m. p. 115-117°. Yield: 90%.

Found %: N 3.84. Equivalents 1.00. C$_{14}$H$_{17}$O$_5$NSP$_2$. Calculated %: N 3.72. Equivalents 1.00.

P,P-Diethyl P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid (IX, R = C$_6$H$_5$) was prepared analogously to the preceding compound. Yield: 81%. M. p. 67-69° (from a mixture of carbon tetrachloride and petroleum ether).

Found %: N 3.38. Equivalents 1.01. C$_{16}$H$_{21}$O$_5$NSP$_2$. Calculated %: N 3.49. Equivalents 1.00.

Tetraphenyl ester of thionoimidodiphosphoric acid (IX, R = C$_6$H$_5$). A. From P,P-dichloride of P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid. The tetra ester was prepared analogously to the tetraphenyl ester of imidodiphosphoric acid (method A). Yield: 87%. M. p. 100-102° (from a mixture of benzene and petroleum ether).

Found %: N 3.02. Equivalents 1.00. C$_{24}$H$_{21}$O$_5$NSP$_2$. Calculated %: N 2.82. Equivalents 1.00.

B. From diphenyl ester of trichlorophosphazothionophosphoric acid. The tetra ester was prepared analogously to the tetraphenyl ester of imidodiphosphoric acid (method B). Yield: 53%. M. p. 100-102° (from a mixture of benzene and petroleum ether). The product did not give a depression in mixed melting point with the substance prepared by method A.

P,P-Diphenyl P',P'-di-p-chlorophenyl ester of P-thionoimidodiphosphoric acid (IX, R = p-ClC$_6$H$_4$). To a solution of 0.03 mole of sodium methoxide in 20 ml of methanol there was added 0.03 mole of p-chlorophenol, the methanol was distilled in vacuo and to the dry sodium p-chlorophenoxide there was added the solution of 0.01 mole of (II) in 20 ml of benzene. The mixture was refluxed for 2 hrs, washed with water, the benzene layer was separated and benzene was distilled in vacuo. To the residue there was added 20 ml of N solution of sodium hydroxide in methanol. The mixture was refluxed for 1 hr, poured into water and acidified. The separated oil was removed from water by decantation and was treated with a small volume of methanol, after which it crystallized. The crystals were filtered off and recrystallized from alcohol. Needles, m. p. 144-146°. Yield: 34%.

Found %: Cl 12.45. Equivalents 1.00. C$_{24}$H$_{19}$O$_5$NCl$_2$P$_2$S. Calculated %: Cl 12.54. Equivalents 1.00.

P,P-Di-p-nitrotetraphenyl ester of P'-thionoimidodiphosphoric acid (IX, R = C$_6$H$_4$NO$_2$-p). A. From diphenyl ester of tri-p-nitrophenoxyphosphazothionophosphoric acid. A mixture of 0.02 mole of the ester and 20 ml of 2 N solution of sodium hydroxide in methanol was refluxed for 10 min. The resulting yellow homogeneous solution was poured into water and acidified. The resulting oil was separated from water by decantation and was triturated with methanol. The crystalline precipitate was filtered off and recrystallized from alcohol. Yield: 12%. M. p. 174-76°.

Found %: N 7.12. C$_{24}$H$_{19}$O$_9$N$_3$SP$_2$. Calculated %: N 7.15.

B. From P,P-dichloride of P',P'-diphenyl ester of P'-thionoimidodiphosphoric acid. A mixture of 0.01 mole mole of (IV), 15 ml of dioxane and 0.03 mole of anhydrous sodium p-nitrophenoxide was refluxed until the p-nitrophenoxide had disappeared, after which it was poured into water and acidified. The resulting oil was separated from water by decantation and was treated with a small volume of methanol. The resulting crystalline precipitate was washed and recrystallized from alcohol. The purified product melted at 174-176° and did not give a depression in mixed melting point with the substance prepared by method A.

## SUMMARY

1. It was shown that diphenyl phosphoramidate and diphenyl thionophosphoramidate react with phosphorus pentachloride, forming trichlorophosphazo compounds thereby.

2. The hydrolysis of the trichlorophosphazo compounds, their reactions with aniline, alcoholates and phenoxides were studied.

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# DIRECT AZO DYES — DERIVATIVES OF
## 1,8-NAPHTHOYLENE-1',2'-BENZIMIDAZOLE

B. M. Krasovitskii, R. M. Matskevich, N. A. Radochina,
and K. P. Riazanova

The positive effect which is directed to the substantivity of dyes by the presence of the imidazole ring in their molecules had been noted a long time ago [1-3]. In continuation of these studies, B. A. Porai-Koshits and Ch. Frankovskii recently prepared some disazo dyes — derivatives of benzimidazole, which are well fixed by the cotton fiber [4]. Some years ago we had prepared some monoazo dyes from 1,8-naphthoylene-4'-amino-1',2'-benzimidazole (I) and 1,8-naphthoylene-5'-amino-1',2'-benzimidazole (II); these azo dyes were tested as acid dyes [5].



(I)        (R — azo component)        (II)
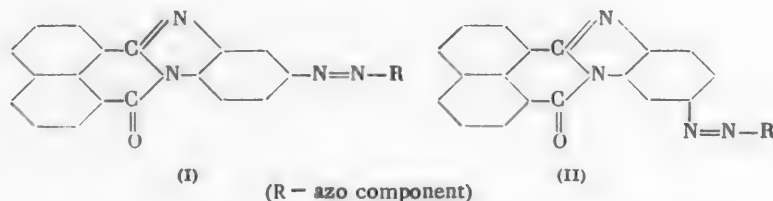
The goal of the present study is the synthesis of monoazo dyes which are isomeric with the previously prepared dyes (I) and (II), with the azo group being in the naphthalene nucleus of the structure of naphthoylenebenzimidazole, and of disazo dyes which contain azo groups both in the benzene and the naphthalene nuclei of this structure.

We used 4-nitronaphthalic anhydride, as the starting material for the preparation of the monoazo dyes; the substance was converted, by condensation with o-phenylenediamine, into the corresponding nitro derivative of 1,8-naphthoylene-1',2'-benzimidazole; the latter was reduced to the amine, which then served as the azo component for the azo dyes. In the reaction of 4-nitronaphthalic anhydride with o-phenylenediamine there is possible the formation of two isomeric products (III) and (IV).



(III)        (IV)
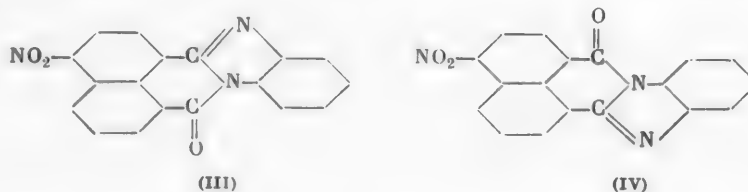
A chromatographic examination of the monoazo dyes prepared by us showed their homogeneity, which fact evidently testifies that the reaction of 4-nitronaphthalic anhydride with o-phenylenediamine yields but one product. The studies carried out by us at an earlier date [5, 6] permitted us to express some considerations about the mechanism of the process of formation of 1,8-naphthoylene-1',2'-benzimidazole from naphthalic anhydride and aromatic o-diamines [6]. Our experimental data agree very well with the supposition that during the reaction of

naphthalic anhydride with o-diamines the formation of the imidazole ring takes place before that of the imide ring.
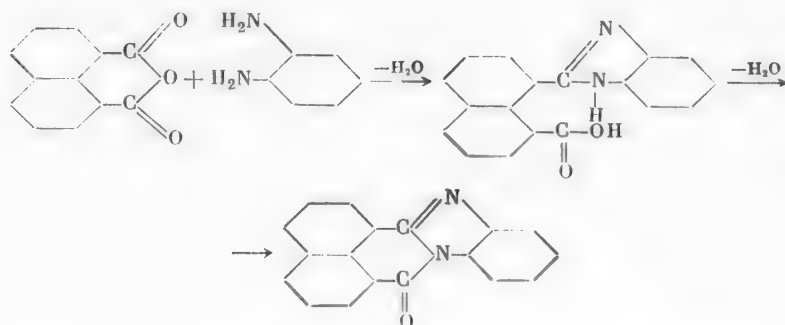
On the basis of studies [7] it is possible to consider that in the first stage of this process there is formed the monoacyl derivative of the o-diamine. Then, commencing with the suppositions developed by B. A. Porai-Koshits [8], it is possible to suppose that this monoacyl derivative suffers the following changes: as the result of intrusion of the unshared electron pair of nitrogen of the amino group into the electron deficiency at the carbon atom of the carbonyl group, there is formed the addition product which after an intramolecular rearrangement and loss of a molecule of water is transformed into the derivative of naphthalenemonocarboxylic acid containing the imidazole ring; this substance, in turn, by losing a molecule of water is transformed into 1,8-naphthoylene-1',2'-benzimidazole.
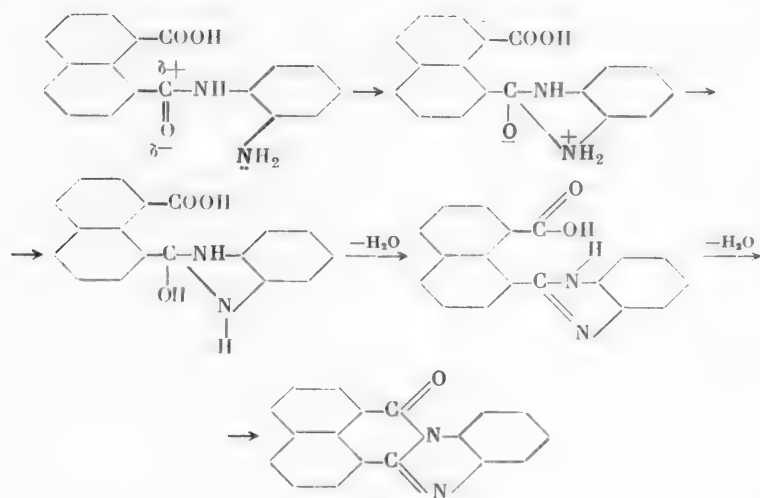
By using this scheme for the consideration of the reaction between 4-nitronaphthalic anhydride and o-phenylenediamine, we may make a supposition about the structure of the product that is formed thereby. In the molecule of 4-nitronaphthalic anhydride one of the carbonyl groups is bound with the nitro group by a shorter chain of conjugated double bonds than the other carbonyl group. Electronic deficiency at the carbon atom of this carbonyl group should be greater, owing to the electron-acceptor action of the nitro group, than that at the carbon atom of the other carbonyl; therefore, one may expect the formation of a nitro product having the structure (III). In this case, the dyes formed from this nitro compound should have the structure (V). These monoazo dyes have considerable substantivity to cotton, but are relatively poorly soluble in water and yield uneven color on the cloth.

(V)
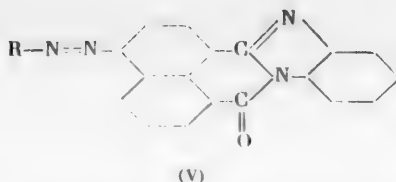
More interesting were the disazo dyes prepared by us. For their preparation we introduced 4-nitronaphthalic anhydride into a reaction with 1,2-diamino-4-nitrobenzene and the resulting product was reduced to the diamine necessary for the preparation of the dyes. In the preparation of the dinitro compound, the formation of four isomers (VI-IX) is theoretically possible.



(VI)



(VII)



(VIII)



(IX)
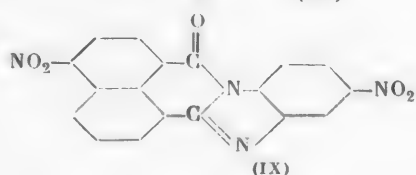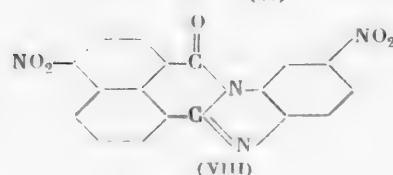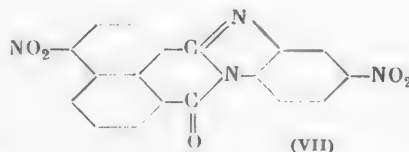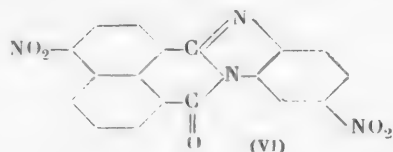
The above considerations about the structure of monoazo dyes testify to the fact that the formation of isomers (VIII) and (IX) is less probable. A chromatographic examination of the disazo dyes prepared by us showed their homogeneity. Consequently, evidently only one of the possible isomers is formed. Since, in the reaction of 4-nitronaphthalic anhydride with 1,2-diamino-4-nitrobenzene, the amino group of the diamine which has the more basic character should react first, one may assign to the product of condensation the structure shown as (VI), while the dyes formed from it may be given the structure of (X).



(X)
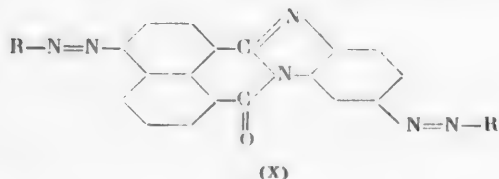
The disazo dyes (the azo components were H- and Chicago SS acids; the coupling was run in basic medium) were readily soluble in water and had high order of substantivity to cotton. These dyes have deeper pigmentation in aqueous solutions than the monoazo dyes for which we had given the structure of (V). Thus, for example, disazo dyes with the azo component of H-acid has the absorption maximum at 560 mμ, while the corresponding monoazo dye has one at 600 mμ.

EXPERIMENTAL

4(5?)-Nitro-1,8-naphthoylene-1',2'-benzimidazole. A mixture of 4-nitronaphthalic anhydride (5 g) and o-phenylenediamine (3 g) was suspended in glacial acetic acid and heated at reflux on a sand bath. During the first 10 min of refluxing there precipitated a dense yellow precipitate, which failed to change after 3 hrs of heating. The resulting precipitate was filtered off and boiled with dilute hydrochloric acid, followed by water, 5% solution of sodium carbonate and again water, for freeing it from admixtures of the starting materials. The yield was 4.4 g (69%).

Found %: N 13.42, 13.28. $C_{18}H_9O_3N_3$. Calculated %: N 13.33.

The resulting substance was a yellow powder which did not have a sharp melting point but which shrank and darkened at 250-257°; it was soluble in the cold in concentrated sulfuric acid, and in hot benzene and methyl alcohol.

4(5?)-Amino-1,8-naphthoylene-1',2'-benzimidazole.   4 g of the nitro compound was suspended in 25 ml of pyridine, heated to boiling, and treated dropwise with 25 ml of N solution of sodium polysulfide in pyridine, the mixture being heated for 15 min and then poured into water;  a red-violet precipitate formed, which was filtered off, washed with water and dried.  The yield was 1.8 g (50%).

Found %:  N 14.40.  $C_{18}H_{11}ON_3$.  Calculated %:  N 14.74.

The substance was a red-violet powder which did not melt at 300°;  it was readily soluble in cold concentrated sulfuric acid, glacial acetic acid and methyl alcohol.

Condensation of 4-nitronaphthalic anhydride with 1,2-diamino-4-nitrobenzene.   A well triturated mixture of 6 g of 4-nitronaphthalic anhydride and 3.6 g of 1,2-diamine-4-nitrobenzene was heated for 1 hr on an oil bath, preheated to 185°.  The mixture darkened at first, then began to melt.  After being cooled, the reaction product was washed free of the starting materials by repeated boiling with dilute hydrochloric acid, then with 5% solution of sodium carbonate.  The yield was 7.8 g (88%).

Found %:  N 15.43, 15.46.  $C_{18}H_8O_5N_4$.  Calculated %:  N 15.55.

The product was a yellow powder with m. p. 261° (after reprecipitation with water from a pyridine solution), which was readily soluble in pyridine and in hot methyl alcohol and glacial acetic acid.

Reduction of dinitro compound.   2 g of the dinitro compound in 40 ml of methyl alcohol was heated on a water bath to boiling under a reflux condenser, treated with 20 ml of water and under continued refluxing was gradually treated with 10 g of sodium hydrosulfite.  The nitro compound went into solution during the addition of the hydrosulfite and the solution gradually changed its color from yellow to dark red.  After the addition of the entire amount of the hydrosulfite, the refluxing was continued for 1 hr longer, after which the solution was filtered and the filtrate was evaporated nearly to dryness.  After addition of concentrated hydrochloric acid there formed a precipitate of bright red crystals of the hydrochloride of the amine.  The free base was liberated by the addition of ammonium hydroxide to the aqueous solution of the hydrochloride.  The resulting amine was a dark brown powder with m. p. 360°, which was soluble in acetic acid, alcohol and dilute hydrochloric acid.  The presence of the 1,8-naphthoylene-1',2'-benzimidazole grouping and the two amino groups in the resulting product was confirmed by deamination and the synthesis of the dibenzoyl derivative.

The deamination was run as follows:  0.2 g of the amine was dissolved in dilute hydrochloric acid and, after cooling the solution to 0°, there was added to it the calculated amount of sodium nitrite, after which there was added 2 g of potassium hypophosphite ($KH_2PO_2$) with good stirring.  The mixture was set aside for one day, after which the resulting precipitate was filtered off and washed with 3% solution of alkali and water, following which it was recrystallized from glacial acetic acid.  The resulting product melted at 188°, which corresponded to the melting point of 1,8-naphthoylene-1',2'-benzimidazole [7].

The dibenzoyl derivative of the diamine, prepared by us by the Schotten-Baumann method, was a substance with red color and m. p. 238-239°;  it was soluble in hot alcohol, acetic acid and pyridine, and insoluble in water.

Found %:  N 10.82, 10.95.  $C_{32}H_{20}O_3N_4$.  Calculated %:  N 11.02.

Mono- and disazo dyes — derivatives of 1,8-naphthoylene-1',2'-benzimidazole.   Since 4(5?)-amino-1,8-naphthoylene-1',2'-benzimidazole is insoluble in dilute hydrochloric acid, we diazotized it by means of nitrosyl sulfuric acid:  the sample of the amine was dissolved in excess concentrated sulfuric acid and to this solution there was added the calculated amount of dry sodium nitrite.  The mixture was stirred well until the complete dissolution of sodium nitrite had taken place after which the solution was poured on ice.  The diamino derivative of 1,8-naphthoylene-1',2'-benzimidazole was diazotized in the conventional manner by addition of the calculated amount of sodium nitrite to the hydrochloric acid solution of the amine.  The coupling of the diazo compounds with H- and Chicago SS-acids was performed in an alkaline medium, which was maintained by addition of sodium carbonate.  The dyes were purified by the acetate method [9] and by chromatography on aluminum oxide.  The absorption maxima of the aqueous solutions of the dyes were determined with the model SF-2 m spectrophotometer.

## SUMMARY

There were prepared the direct mono- and disazo dyes — derivatives of 1,8-naphthoylene-1',2'-benzimidazole;  a supposition was expressed concerning the structure of these dyes.

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•  Original Russian pagination.  See C. B. translation.

# REPLACEMENT OF HALOGEN IN AZO COMPOUNDS

## III. PREPARATION OF DERIVATIVES OF o-ARYLALKOXYANILINES

B. I. Stepanov and M. A. Andreeva

The replacement of the chlorine atom in 2-chlorophenylazo-2'-naphthol for arylalkoxy groups is accomplished with great ease under conditions which are close to those for the replacement of chlorine by an alkoxy group [1] — in the reaction with the alcoholate in an excess of the corresponding alcohol in the presence of a copper salt at temperature about 100°. In this manner there were prepared the products of replacement of chlorine by phenylmethoxy group — by reaction with sodium benzyloxide, by β-phenylethoxy group — by reaction with sodium β-phenylethoxide, and by γ-phenylpropoxy group — by reaction with sodium γ-phenylpropoxide. The resulting arylalkoxy substituted dyes were capable of dyeing the acetate and the polyamide fibers. The corresponding o-arylalkoxyanilines were prepared by reductive cleavage of the indicated dyes.

O(CH₂)ₙC₆H₅
—N=N—
OH
n = 1, 2, 3
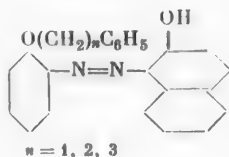
## EXPERIMENTAL

Replacement of chlorine by phenylmethoxy-, β-phenylethoxy, and γ-phenylpropoxy groups. 8 g of the azo dye from 2-chloroaniline and 2-naphthol (m. p. 167°), triturated with 4 g of copper sulfate and 5 ml of water, was introduced into the solution of sodium alcoholate prepared by the reaction of 2 g of metallic sodium with 40 ml of the appropriate alcohol (benzyl — b. p. 204-206°; β-phenylethyl — b. p. 219-221° at 750 mm, γ-phenylpropyl — b. p. 235-237°). The mixture was heated under a reflux condenser for 8 hrs at 100-103°, after which it was diluted with 2-3 volumes of methyl alcohol. The resulting precipitate was filtered off, boiled with 100 ml of concentrated hydrochloric acid, refiltered after dilution with water, washed free of chloride ions and dried in air. The test for halogen was negative.

There was obtained 8.65 g (86.3%) of the phenylmethoxy substituted dye (I). After recrystallization from glacial acetic acid it formed bundles of small sharp needles, m. p. 152-153° (see [2]). The dye was soluble in benzene, toluene, chloroform, chlorobenzene and glacial acetic acid, poorly soluble in methyl and ethyl alcohols, and insoluble in water.

There was obtained 9.45 g of phenylethoxy substituted dye (II). After recrystallization from glacial acetic acid it formed narrow flat needles, m. p. 161°. The dye was soluble in benzene, toluene, chloroform, and glacial acetic acid, poorly soluble in methyl and ethyl alcohols, and insoluble in water.

There was obtained 7.5 g (69.3%) of the phenylpropoxy substituted dye (III). After recrystallization from 80% acetic acid, followed by ethyl alcohol, it formed bundles of plates with oval shape; m. p. 136.5-137°. The dye was soluble in benzene, toluene, and glacial acetic acid; it was less soluble in dilute acetic acid and in methyl and ethyl alcohols, and insoluble in water.

Preparation of 2-(β-phenylethoxy)- and 2-(γ-phenylpropoxy)-anilines.* 1 g of the appropriate arylalkoxy substituted dye and 25 ml of water were added to the solution of stannous chloride (prepared from 2 g of metallic tin and 25 ml of concentrated hydrochloric acid) and the mixture was refluxed until it became colorless. The

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* With participation by V. S. Zenkevich.

| Sub-stance | Found (in %) | | | Empirical formula | Calculated (in %) | | |
|---|---|---|---|---|---|---|---|
| | C | H | N | | C | H | N |
| (I) | 77.82, 77.62 | 5.00, 5.20 | 8.11, 8.02 | $C_{23}H_{18}O_2N_2$ | 77.97 | 5.09 | 7.91 |
| (II) | 78.04, 78.13 | 5.42, 5.59 | 7.75 | $C_{24}H_{20}O_2N_2$ | 78.26 | 5.43 | 7.61 |
| | 8.38, 78.30 | 5.91, 5.72 | 7.50 | $C_{25}H_{22}O_2N_2$ | 78.53 | 5.76 | 7.33 |
| (IV) | 67.30, 67.17 | 6.27, 6.52 | 5.50, 5.75 | $C_{14}H_{16}ONCl$ | 67.33 | 6.41 | 5.61 |
| (V) | 79.92, 80.02 | 6.18, 6.05 | 4.66 | $C_{21}H_{19}O_2N$ | 79.49 | 5.99 | 4.41 |
| (VI) | 68.24, 68.11 | 6.91, 6.71 | 5.33, 5.46 | $C_{15}H_{18}ONCl$ | 68.31 | 6.83 | 5.31 |
| (VII) | 79.35, 79.56 | 6.27, 6.45 | 4.47 | $C_{22}H_{21}O_2N$ | 79.76 | 6.34 | 4.23 |

precipitate, which formed on cooling and standing for one day, was filtered off and treated with 25 ml of 5% solution of sodium hydroxide with addition of 0.3 g of sodium hydrosulfite, after which the 2-arylalkoxyaniline was extracted with ether. After treatment of the ethereal layer with 3 ml of concentrated hydrochloric acid there formed a precipitate of the hydrochloride of the amine, which was filtered off, dried in air and recrystallized from dilute methyl alcohol. For the preparation of the N-benzoyl derivative, 0.1 g of the amine hydrochloride was treated with 1 ml of 20% solution of sodium hydroxide and 0.5 ml of benzoyl chloride, after which the mass was diluted with water, the precipitate was filtered off, washed, dried in air and recrystallized from methyl alcohol.

2-($\beta$-Phenylethoxy) aniline hydrochloride (IV) — neeldes, m. p. 181.5-182°.

N-Benzoyl derivative of 2-($\beta$-phenylethoxy) aniline (V) — flat rhomboids, m. p. 110.5-111° (according to literature data [3]: m. p. 113-114°, from ligroine).

2-($\gamma$-Phenylpropoxy) aniline hydrochloride (VI) — large flat needles, m. p. 162.5-163°.

N-Benzoyl derivative of 2-($\gamma$-phenylpropoxy) aniline (VII) — bundles of small needles, m. p. 87-87.5°.

The analytical data of the compounds prepared by us are given in the table.

## SUMMARY

1. By the reaction of sodium alcoholates with the azo dye from 2-chloroaniline and 2-naphthol in the presence of a copper salt, the chlorine atom in the dye was replaced by phenylmethoxy-, $\beta$-phenylethoxy- and $\gamma$-phenylpropoxy groups.

2. 2-($\beta$-Phenylethoxy)- and 2-($\gamma$-phenylpropoxy) anilines were prepared by reductive cleavage of the arylalkoxy substituted dyes.

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[3] A. Sieglitz and H. Koch, Ber. 58, 78 (1925).

* Original Russian pagination. See C. B. translation.

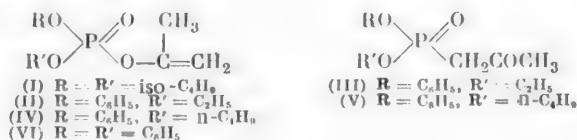# ANOMALOUS REACTION OF PHOSPHITES WITH α-HALO KETONES

## VIII. REACTIONS OF MIXED PHOSPHITES WITH CHLORO- AND DICHLOROACETONES

### A. N. Pudovik and E. G. Chebotareva

It was shown by us in previous publications that α-halo substituted ketones react with complete esters of phosphorous acid both according to the scheme of the Arbuzov rearrangement, forming esters of keto phosphonic acids, and according to the anomalous reaction route with formation of unsaturated esters of phosphoric acid [1]. Both these reactions proceed independently of each other; the ratio of their rates depends on the temperature at which the experiment is performed, the nature of the halogen and its position in the ketone molecule [2]. Lowering of the experimental temperature, change from the iodo- to bromo- and chloroketones, from primary to secondary and tertiary positions of the halogen in the molecule of the halo ketone, all favor the progress of the anomalous reaction. With the presence of more than one chlorine atom in the halo ketone at the α-position, the reactions proceed exclusively or almost exclusively according to the anomalous direction.

We set up for the goal in the present work, a study of the reaction of α-halo ketones with mixed phosphites containing aliphatic or aliphatic and aromatic radicals in the ester groups. For the α-halo ketones we used chloro- and α,α-dichloroacetones. The selection of these halo ketones was made owing to the fact that the reaction of the former with the usual phosphites proceeds predominantly anomalously, while that of the latter proceeds completely anomalously [3]. As is known, the reaction of mixed esters of phosphorous acid with alkyl halides and other halogen containing organic compounds proceeds in such a way that the radical with the smallest molecular weight is cleaved from the phosphite; there are formed the alkyl halide and an ester of a phosphonic acid. It was of some interest to determine the behavior of mixed phosphites in their reactions with α-halo ketones which proceed according to the anomalous scheme. As the mixed phosphites we utilized diisobutyl ethyl, diethyl phenyl, di-n-butyl phenyl esters and ethyl bis-(diethylamido)phosphite, $(Et_2N)_2POEt$.

The diisobutyl isopropenyl ester of phosphoric acid (I) was obtained from the reaction of chloroacetone with diisobutyl ethyl phosphite. In respect to its physical constants this substance was identical with the diisobutyl isopropenyl phosphate, prepared by us earlier from chloroacetone and triisobutyl phosphite [2]. The keto phosphonic ester, isomeric to this, was not isolated in the pure state owing to the low content of it in the reaction mixture. The constants of (I), as well as those of all the other products described below which were prepared from chloroacetone, are shown in Table 1. Two products were obtained from the reaction of chloroacetone with diethyl phenyl phosphite: phenyl ethyl isopropenyl ester of phosphoric acid (II) and phenyl ethyl ester of phosphonoacetone (III). Ethyl chloride was evolved during the reaction.



(I)  R = R′ = iso -$C_4H_9$
(II)  R = $C_6H_5$, R′ = $C_2H_5$
(IV)  R = $C_6H_5$, R′ = n-$C_4H_9$
(VI)  R = R′ = $C_6H_5$

(III)  R = $C_4H_9$, R′ = $C_2H_5$
(V)  R = $C_4H_9$, R′ = n-$C_4H_9$

Three times more of substance (II) than of substance (III) was isolated. The double bond was quantitatively determined in substance (II), while it was absent in substance (III). Acetone was obtained in 90% yield in transesterification of (II) with ethyl alcohol, run in the presence of sodium ethoxide.
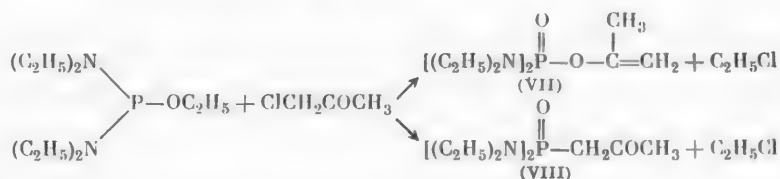
## TABLE 1

Reaction Products of the Mixed Esters with Chloroacetone

| Initial ester | Reaction product | Yield (in %) | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ found | $MR_D$ calc. | Phosphorus content (%) found | Phosphorus content (%) calc. | Content of CO (in %) found | Content of CO (in %) calc. | Double bond found (in %) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $(iso\text{-}C_4H_9O)_2POC_2H_5$ | Diisobutyl isopropenyl phosphate (I) | 69.3 | 122—123°(9.) | 0.9960 | 1.4245 | 64.15 | 64.52 | – | – | – | – | – |
| $(C_2H_5O)_2POC_6H_5$ | Ethyl isopropenyl phenyl phosphate (II) | 58.3 | 151.5—152(10) | 1.1423 | 1.4845 | 60.72 | 60.92 | 12.50 | 12.80 | – | – | 97.6 |
|  | Ethyl phenyl ester of phosphonoacetone (III) | 17.0 | 178—179(8.) | 1.1983 | 1.5005 | 59.99 | 60.27 | 12.43 | 12.80 | 11.53 | 11.56 | – |
| $(C_4H_9O)_2POC_6H_5$ | n-Butyl isopropenyl phenyl phosphate (IV) | 49.2 | 166—167(9) | 1.1005 | 1.4825 | 70.07 | 70.16 | 11.68 | 11.47 | – | – | 96.1 |
|  | n-Butyl phenyl ester of phosphonoacetone (V) | 13.3 | 176—177(4) | 1.1276 | 1.4944 | 69.75 | 69.51 | 11.54 | 11.47 | 10.50 | 10.57 | – |
| $(C_6H_5O)_2POC_4H_9$ | Diphenyl isopropenyl phosphate (VI) | 57.4 | 186(1.5) | 1.2271 | 1.5483 | 75.15 | 75.79 | 10.22 | 10.68 | – | – | 94.2 |
| $[(C_2H_5)_2N]_2POC_2H_5$ | Isopropenyl bis-(diethylamido)-phosphate (VII) | 40 | 124—125(8) | 0.9920 | 1.4520 | 67.53 | 68.23 | 12.69 | 12.50 | – | – | – |
|  | Bis-(diethylamide) of phosphonoacetone (VIII) | 8.3 | 149—150(8) | 1.0413 | 1.4709 | 66.62 | 67.58 | 12.75 | 12.50 | – | – | – |

The reaction of chloroacetone with phenyl di-n-butyl phosphite proceeds analogously. Phenyl butyl isopropenyl ester of phosphoric acid (IV) and phenyl butyl ester of phosphonoacetone (V) were obtained. The presence of the double bond in substance (IV) was confirmed by bromination; acetone was obtained in a quantitative yield on hydrolysis of this substance with 30% sulfuric acid. The carbonyl group was determined in (V). Three times more of substance (IV) was obtained than of substance (V). n-Butyl chloride was isolated in the course of the reaction; about 85% of the theoretical amount of this substance, calculated for both the reaction products, was collected.

During the action of chloroacetone on diphenyl n-butyl ester of phosphorous acid there was obtained the diphenyl isopropyl ester (VI). The diphenyl ester of phosphonoacetone did form, but in a small amount, and could not be isolated in the pure state. Formaldehyde, identified as the product of condensation with dimethylcyclohexanedione, was obtained in ozonization of ester (VI).

The reaction of chloroacetone with the ethyl ester of bis-(diethylamido)phosphite proceeded just as readily as with the mixed phosphites. There were isolated: isopropenyl ester of bis-(diethylamido)phosphoric acid (VII) and bis-(diethylamido)phosphonoacetone (VIII). Ethyl chloride was evolved in the process of the reaction.

$$
\begin{array}{c}
(C_2H_5)_2N \\
\diagdown \\
P-OC_2H_5 + ClCH_2COCH_3 \\
\diagup \\
(C_2H_5)_2N
\end{array}
\xrightarrow{}
\begin{array}{c}
\overset{O}{\overset{\|}{[(C_2H_5)_2N]_2P}}-O-\overset{\overset{CH_3}{|}}{C}=CH_2 + C_2H_5Cl \\
(VII) \\[2mm]
\overset{O}{\overset{\|}{[(C_2H_5)_2N]_2P}}-CH_2COCH_3 + C_2H_5Cl \\
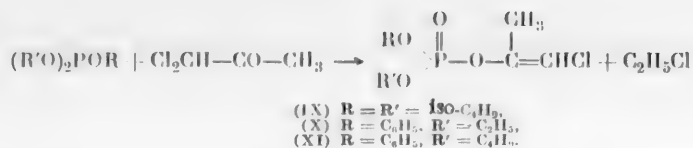(VIII)
\end{array}
$$

The presence of the double bond in substance (VII) was confirmed by bromination, while it was absent in substance (VIII). Five times more of substance (VII) than of substance (VIII) was isolated.

Then we studied the reactions of diisobutyl ethyl phosphite, diethyl phenyl phosphite and di-n-butyl phenyl phosphite with $\alpha,\alpha$-dichloroacetone. As in the case of the usual phosphites, the reactions proceeded in these cases solely by the anomalous route with formation of the corresponding unsaturated phosphoric acid esters.
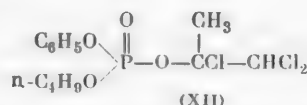
TABLE 2

Reaction Products of Mixed Esters with $\alpha,\alpha$-Dichloroacetone

| Initial ester | Reaction product | Yield (%) | Boiling point (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | $MR_D$ | | Phosphorus content (%) | | Chlorine content (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | found | calc. | found | calc. | found | calc. |
| (iso-$C_4H_9O)_2PO$ $C_2H_5$ | Diisobutyl chloro-isopropenyl phosphate (IX) | 63.3 | 139.5—140°(9) | 1.0855 | 1.4402 | 69.16 | 69.39 | 10.71 | 10.88 | 12.39 | 12.47 |
| $(C_2H_5O)_2POC_6H_5$ | Ethyl chloro-isopropenyl phenyl phosphate (X) | 51.5 | 130—131 (1) | 1.2446 | 1.4972 | 65.60 | 65.79 | 11.1 | 11.20 | 12.40 | 12.83 |
| $(C_4H_9O)_2POC_6H_5$ | n-Butyl chloro-isopropenyl phenyl phosphate (XI) | 61.4 | 155—156 (3) | 1.1800 | 1.4917 | 74.89 | 75.02 | 10.25 | 10.17 | 11.50 | 11.65 |

2529

$$(R'O)_2POR + Cl_2CH-CO-CH_3 \longrightarrow \begin{matrix} RO \\ \diagdown \\ RO \end{matrix} \overset{\overset{O}{\parallel}}{P}-O-\overset{\overset{CH_3}{|}}{C}=CHCl + C_2H_5Cl$$

(IX)  R = R' = iso-$C_4H_9$,
(X)  R = $C_6H_5$, R' = $C_2H_5$,
(XI)  R = $C_6H_5$, R' = $C_4H_9$.

The constants of the products obtained (IX-XI) and the results of their analyses for the content of phosphorus and chlorine are shown in Table 2.

Trichloroisopropyl butyl phenyl ester of phosphoric acid (XII) was obtained in the chlorination of chloroisopropenyl n-butyl phenyl ester of phosphoric acid (XI).

$$\begin{matrix} C_6H_5O \\ \diagdown \\ n\text{-}C_4H_9O \end{matrix} \overset{\overset{O}{\parallel}}{P}-O-\overset{\overset{CH_3}{|}}{C}Cl-CHCl_2$$
(XII)

It is possible to draw the conclusion from this work that the mixed esters of phosphorous acid behave similarly both in the reactions of the Arbuzov rearrangement and in the anomalous reaction with $\alpha$-halo ketones; the radical with the smallest molecular weight participates in the formation of the alkyl halide.

## EXPERIMENTAL

Mixed esters of phosphorous acid were prepared from the corresponding ester chlorides of phosphorous acid and alcohols, in the presence of pyridine.

The technique of running the reactions of chloro- and dichloroacetone with mixed phosphites. To 30-40 g of the mixed phosphite, placed in an Arbuzov flask and preheated to 120-140°, there was gradually added from a dropping funnel the equimolar amount of chloro- or dichloroacetone. The Arbuzov flask was connected to a distilling condenser. In cases in which ethyl chloride was evolved in the process of the reaction, this was passed through a glass tube coil cooled with a freezing mixture and collected in a receiver. After the addition of chloro-acetone or dichloroacetone, the reaction mixture was heated for 1 hr longer at 120-130° after which it was distilled in vacuo from a flask with a Widmer column. The constants of all the products thus obtained and their analyses are shown in Tables 1 and 2.

Transesterification of ethyl phenyl isopropenyl esters of phosphoric acid. To a solution of sodium ethoxide, prepared in an Arbuzov flask, from 10 ml of anhydrous ethyl alcohol and 0.17 g of sodium, there was added 9.3 g of ethyl phenyl isopropenyl phosphate. After heating of the reaction mixture on a water bath, there was collected 1.9 g of acetone. Its semicarbazone had m. p. 187-188°. The mixed melting point with an authentic sample showed no depression.

Hydrolysis of n-butyl phenyl isopropenyl ester of phosphoric acid. n-Butyl phenyl isopropenyl phosphate (4.5 g) and 8 ml of 30% sulfuric acid, placed in an Arbuzov flask provided with a distilling condenser, were gradually heated on a water bath. The reaction began immediately and proceeded very vigorously with strong heat evolution within the reaction mixture. There was collected 1.5 g of acetone with b. p. 56-57°. Its semicarbazone had m. p. 188°.

Ozonolysis of diphenyl isopropenyl phosphate. Ozonized oxygen was passed for 20 hrs into a solution of 4 g of diphenyl isopropenyl phosphate in 20 ml of dry carbon tetrachloride with cooling by means of a freezing mixture. After the removal of the solvent by evacuation, the ozonide was decomposed with water, with heating on a water bath. From the distillate, which had the sharp odor of formaldehyde, there was obtained the condensation product with dimethylcyclohexanedione, with m. p. 188-189°. The mixed melting point with an authentic sample had m. p. 189°.

Chlorination of chloroisopropenyl n-butyl phenyl ester of phosphoric acid. Chlorine was slowly introduced into a solution of 6.2 g of the phosphate ester in 30 ml of dry carbon tetrachloride with cooling by means of a freezing mixture. The solution remained colorless during the process of chlorination, but turned yellow upon

reaching the theoretical weight gain of 1.12 g. After distillation of the reaction mixture from a flask with a Widmer column there was obtained 4.8 g of $\alpha,\beta,\beta$-trichloroisopropyl n-butyl phenyl phosphate.

B. p. 180-181° at 4 mm, $d_4^{20}$ 1.2837, $n^{20}$D 1.5020, $MR_D$ 87.36; calc. 85.22. Found %: P 8.30; Cl 28.48. $C_{13}H_{18}O_4Cl_3P$. Calculated %: P 8.25; Cl 28.32.

## SUMMARY

1. The reactions of chloro- and dichloroacetones with diisobutyl ethyl, diethyl phenyl, di-n-butyl phenyl, diphenyl n-butyl esters of phosphorous acid and ethyl bis-(diethylamido)phosphite were studied.

2. The reactions of chloroacetone with mixed esters proceed by two paths: by the anomalous route with formation of unsaturated phosphoric esters and by the scheme of Arbuzov rearrangement with formation of dialkyl esters of phosphonoacetone. The reactions with $\alpha,\alpha$-dichloroacetone proceed exclusively by the anomalous route with formation of unsaturated phosphoric esters.

3. In all the reactions of chloro- and dichloroacetones with mixed esters of phosphorous acid, the alkyl radical of the mixed phosphite having the smallest molecular weight takes part in the formation of the alkyl chloride.

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# ADDITION OF AMMONIA AND AMINES TO ISOPRENE OXIDE

## A. N. Pudovik and I. M. Aladzheva

It was shown in a paper by one of us and S. G. Denislamova [1] that isoprene oxide, in contrast to oxides of propylene [2], isobutylene [3] and butadiene [4], adds alcohols in the presence of alcoholates of the alkali metals predominantly, but not exclusively, in accord with the Markovnikov rule [5]. Some 10-14% of ethers of tertiary alcohols were isolated along with the primary ethers. It appeared interesting in connection with the previous studies to investigate the addition of ammonia and amines to isoprene oxide.

Krasusskii [6] had shown that the addition of ammonia and amines to oxides of unsymmetric ethylenic hydrocarbons — propylene, isobutylene, trimethylethylene and diethylethylene — proceeds according to the Markovnikov rule. Analogous reactions with oxides of diene hydrocarbons have not been studied sufficiently. According to the existing data, ammonia adds to butadiene oxide with formation of a mixture of both isomeric amino alcohols [7], while amines yield amino alcohols with the secondary alcohol grouping only [8]. According to the existing concepts, the order of addition of neutral or basic reagents to unsymmetric $\alpha$-oxides is determined to a considerable degree by polarization of the oxide molecule and by stability of carbon-oxygen bonds in it [9]. In accord with this, one may suppose that the addition of ammonia and amines to isoprene oxide, which is an unsymmetric disubstituted oxide, would proceed in accordance with the Markovnikov rule.

We studied the addition of ammonia, ethylamine, diethylamine and aniline to isoprene oxide. In order to secure a more correct conception of the direction of the course of these reactions, these were run with considerable amounts of isoprene oxide (0.8-1.1 mole), i. e., several times larger than those used previously in analogous experiments with butadiene oxide and some other oxides.

As the result of addition of ammonia to isoprene oxide in aqueous medium there were obtained four products, of which the first two were isomeric products of addition of one molecule of ammonia to one molecule of isoprene oxide, the third was the product of addition of ammonia to two, and the fourth — to three molecules of isoprene oxide.

$$CH_2=CH-\underset{\underset{O}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2 + NH_3 \rightarrow CH_2=CH-\overset{\overset{CH_3}{|}}{C}(OH)-CH_2NH_2 + \\ (I)$$

$$+ CH_2=CH-\underset{\underset{NH_2}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2OH + \left( CH_2=CH-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2 \right)_2 NH + \left( CH_2=CH-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2 \right)_3 N \\ (II) \qquad\qquad (III)$$
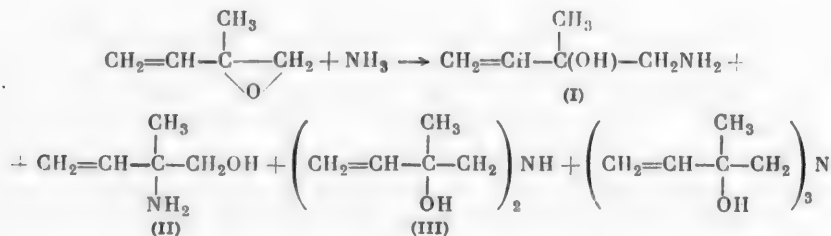
There was obtained approximately 4.5 times more 3-methyl-4-amino-1-buten-3-ol than 3-methyl-3-amino-1-buten-4-ol (II); it boiled 20° lower and had a lower index of refraction and specific gravity. On the basis of a quantitative comparison of the resulting isomers and their physical constants, we came to the conclusion that substance (I) was the amino alcohol with a tertiary alcohol group, i. e., the product formed in accordance with the Markovnikov rule, while substance (II) was the amino alcohol isomeric to it. The product of addition of ammonia to three molecules of isoprene oxide was not isolated in pure state. The characterization of the products obtained

by us is shown in the table. The total yield of amino alcohols, calculated on the isoprene oxide taken for the reaction, was about 60%. In ozonolysis of (II) formaldehyde was identified, which fact also serves as a confirmation of the proposed structural formula and excludes the supposition about the possibility of an allylic shift in the process of reaction, changing (I) into 3-methyl-4-amino-2-buten-1-ol.
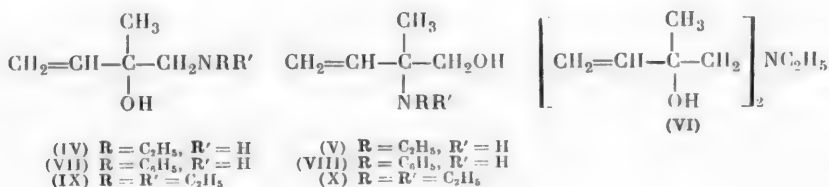
Amino Alcohols Prepared in the Reaction of Isopropene Oxide with Ammonia and Amines

| Reagent | Reaction products | Yield (in %) | Boiling point (pressure in mm) | $d^{20}_4$ | $n^{20}D$ | $MR_D$ | | Nitrogen cont. (in %) | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | found | calc. | found | calc. |
| Ammo- nia | 1-Amino-2-hydroxy-2-methyl-3-butene (I) | 41.0 | 63° (9) | 0.9548 | 1.4692 | 29.51 | 29.77 | 13.78 | 13.86 |
| | 1-Hydroxy-2-amino-2-methyl-3-butene (II) | 9.1 | 83 (13) | 0.9693 | 1.4772 | 29.50 | 29.77 | 13.75 | 13.86 |
| | Bis-(2-hydroxy-2-methyl-3-butenyl)amine (III) | 9.0 | 133.7—134.2 (14) | 0.9702 | 1.4740 | 53.67 | 54.09 | 7.28 | 7.56 |
| Ethyl- amine | 1-Ethylamino-2-hydroxy-2-methyl-3-butene (IV) | 44.4 | 51.5 (9) | 0.8865 | 1.4462 | 38.88 | 39.18 | 10.64 | 10.85 |
| | 1-Hydroxy-2-methyl-2-ethylamino-3-butene (V) | 9.3 | 82 (9) | 0.9157 | 1.4598 | 38.63 | 39.18 | 11.04 | 10.85 |
| | Bis-(2-hydroxy-2-methyl-3-butenyl)ethylamine (VI) | 4.8 | 125—127 (14) | 0.9562 | 1.4730 | 62.38 | 63.67 | 6.96 | 6.57 |
| Phenyl- amine | 1-Phenylamino-2-hydroxy-2-methyl-3-butene (VII) | — | 120—124 (11) | 1.0154 | 1.5470 | 55.67 | 56.23 | 8.18 | 7.90 |
| | 1-Hydroxy-2-phenylamino-2-methyl-3-butene (VIII) | — | 137—140 (11) | 1.0338 | 1.5670 | 56.35 | 56.23 | 8.19 | 7.90 |
| Diethyl- amine | 1-Diethylamino-2-hydroxy-2-methyl-3-butene (IX) | 48.8 | 63 (13) | 0.8534 | 1.4388 | 48.45 | 48.76 | 9.2 | 8.9 |
| | 1-Hydroxy-2-diethylamino-2-methyl-3-butene (X) | 10.5 | 78 (12) | 0.8693 | 1.4472 | 48.36 | 48.76 | 9.0 | 8.9 |

In running the reaction between isoprene oxide and ethylamine, three products were isolated: two isomeric amino alcohols formed by the addition of ethylamine to the oxide ring in both possible directions and the product of addition of ethylamine to two molecules of isoprene oxide. There was obtained 5 times more 3-methyl-4-ethylamino-1-buten-3-ol (IV) than 3-methyl-3-ethylamino-1-buten-4-ol (V). The total yield of products was about 59% (see Table).

The reaction of isoprene oxide with aniline proceeds very slowly and incompletely in an aqueous medium, owing to the low solubility of aniline in water. Two isomeric amino alcohols (VII and VIII) were isolated in low yields.

Addition of a secondary amine — diethylamine — to isoprene oxide proceeded in aqueous medium as readily as that of primary amines. Five times more amino alcohol with the tertiary alcohol group (IX) was formed in comparison with its isomer (X).

$$CH_2=CH-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2NRR' \qquad CH_2=CH-\underset{\underset{NRR'}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2OH \qquad \left[ CH_2=CH-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_2 \right]_2 NC_2H_5$$

(IV) R = C₂H₅, R' = H      (V) R = C₂H₅, R' = H      (VI)
(VII) R = C₆H₅, R' = H      (VIII) R = C₆H₅, R' = H
(IX) R = R' = C₂H₅      (X) R = R' = C₂H₅

The characterization of the prepared substances is given in the Table.

Formation of two isomeric amino alcohols in all the reactions studied by us indicates that the addition of ammonia and amines to isoprene oxide proceeds not only in accordance with the Markovnikov rule, but also to a considerable degree (about $1/5$) contrary to it, i. e., according to an anomalous reaction. Approximately twice as much anomalous products of addition was formed in the reactions studied by us as compared with the amount of anomalous products formed in the reactions of isoprene oxide with alcohols, in the presence of alcoholates [1].

For realization of an alternate synthesis of the amino alcohols, we ran the reaction of isoprene oxide with hydrogen chloride to prepare the original chlorohydrin. The reaction proceeded in an ethereal solution with cooling. We failed to isolate the chlorohydrin in the pure state; along with a considerable amount of tar there was isolated a small fraction with b. p. 53-58° at 13 mm, $n^{20}D$ 1.4732, $d_4^{20}$ 1.0853, which rapidly darkened in air. The chlorine content in this fraction (in two experiments) differed from that calculated for the chlorohydrin by 2-3%. No individual product could be isolated after its reaction with ammonia. In experiments on addition of hydrobromic acid to isoprene oxide, the latter isomerized into tiglic aldehyde [10].

The results obtained by us on the addition of alcohols to isoprene oxide in the presence of alcoholates of the alkali metals, as well as of ammonia and amines, lead to the conclusion that considerable differences exist in the behavior of the oxide of isoprene as compared to oxides of isobutylene and butadiene under analogous conditions. It is necessary to add, however, that for a more correct conception of the course of the reactions of unsymmetric $\alpha$-oxides with nucleophilic reagents in a basic medium, it would be rational to repeat some of the reactions run previously, to repeat them with considerably greater amounts of reagents.

## EXPERIMENTAL

Isoprene $\alpha$-oxide was prepared by oxidation of isoprene with acetyl hydroperoxide in ethereal solution [11]; b. p. 79-81°, $n^{20}D$ 1.4172.

Isoprene oxide (70-90 g) was added dropwise with energetic stirring by a mechanical stirrer to a three-fold (molar) excess of ammonia or amine, dissolved in water. The stirring was usually continued for one day until the oxide layer dissolved completely. (A considerable amount of aniline and oxide failed to react in the reaction with aniline). Ammonia or amine was at first distilled from the solution by gentle heating, after which water distillation was performed in vacuo. The residue was fractionated from a flask with a small Widmer column. The individual fractions, obtained in small amounts, were distilled from flasks with a shortened Widmer column. The constants, analytical results and yields of the products obtained by us are shown in the table.

## SUMMARY

1. It was shown that ammonia, ethylamine and diethylamine add to isoprene oxide predominantly but not exclusively in accordance with the Markovnikov rule. About 20% of amino alcohols containing a primary alcoholic group is formed in comparison with the amount of amino alcohols which contain the tertiary alcoholic group.

2. Products of addition of ammonia and amines to isoprene oxide were obtained and characterized.

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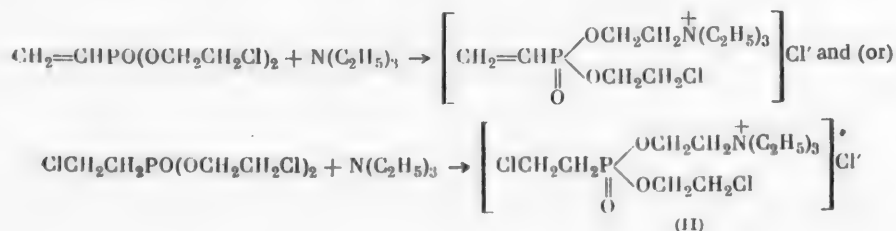# THE PROBLEM OF SYNTHESIS OF DI-β,β'-CHLOROETHYL ESTER
## OF VINYLPHOSPHONIC ACID

### E. L. Gefter

Esters of vinylphosphonic acid are rather reactive compounds, capable of polymerization [1, 2], addition of substances with a mobile hydrogen to the double bond [3-5], participation in diene synthesis [6], etc. One of the insufficiently studied compounds in this series, which became industrially important recently [7], is bis-β,β'-chloroethyl ester of vinylphosphonic acid, prepared first by M. I. Kabachnik [1] by the reaction of alcoholic alkali with bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid. However, this method has a material defect: along with the cleavage of hydrogen chloride, some hydrolysis of the ester takes place, which fact sharply lowers the yields of the ester of vinylphosphonic acid.

In order to raise the yields of bis-β,β'-chloroethyl vinylphosphonate we used as dehydrochlorinating agent the triethylamine which was first used by Ford-Moore and Williams [8] in the preparation of diethyl vinylphosphonate by the principle mentioned above. Since the halogen in the β-haloethyl group bound directly to phosphorus is more active than the halogen in a similar group bound to phosphorus through oxygen [1], we supposed that the dehydrochlorination should occur only in the acidic part of the molecule of bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid. However, it appeared that this process proceeds in a more complex manner. Along with the expected reaction product — bis-β,β'-chloroethyl vinylphosphonate — obtained in 50-60% yields, there also remained always a certain amount of unreacted starting material. In case of utilization of an excess of triethylamine (up to 20% of theoretical), the yields of bis-β,β'-chloroethyl vinylphosphonate declined. It was possible to suppose that the reaction of bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid with triethylamine proceeds in two steps.

1) Formation of an unstable complex or quaternary ammonium salt (addition product I) (formation of complexes in the reactions of tertiary amines with various halogen containing compounds has been described [9, 10]). 2) Facile cleavage of product (I):

$$ClCH_2CH_2PO(OCH_2CH_2Cl)_2 + N(C_2H_5)_3 \rightarrow Cl^-[(C_2H_5)_3N-CH_2CH_2PO(OCH_2CH_2Cl)_2] \rightarrow$$

$$(I)$$

$$\rightarrow CH_2=CHPO(OCH_2CH_2Cl)_2 + N(C_2H_5)_3 \cdot HCl$$
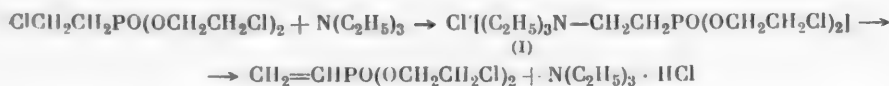
At temperatures of the order of 80-90° other processes occur evidently at a noticeable rate as well; formation of complexes at the chlorine atoms which are present in the alcoholic part of the molecule (addition product II):

$$CH_2=CHPO(OCH_2CH_2Cl)_2 + N(C_2H_5)_3 \rightarrow \left[ CH_2=CHP\overset{O}{\underset{\parallel}{\diagdown}}\begin{matrix}OCH_2CH_2\overset{+}{N}(C_2H_5)_3\\OCH_2CH_2Cl\end{matrix} \right] Cl^- \text{ and (or)}$$

$$ClCH_2CH_2PO(OCH_2CH_2Cl)_2 + N(C_2H_5)_3 \rightarrow \left[ ClCH_2CH_2P\overset{O}{\underset{\parallel}{\diagdown}}\begin{matrix}OCH_2CH_2\overset{+}{N}(C_2H_5)_3\\OCH_2CH_2Cl\end{matrix} \right] Cl^-$$

$$(II)$$

Compounds of type (II) are rather stable [11] and under the reaction conditions may simply precipitate, thus leaving the reaction zone. (Analysis showed the admixture of organophosphorus compounds in the triethylamine hydrochloride.) As a result of such secondary processes, the yields of bis-β,β'-chloroethyl vinylphosphonate should decline naturally, while a part of the starting material would remain unchanged since no free triethylamine would be present in the system.

We supposed that an elevation of the temperature of the system should aid the formation of all the complexes listed above, while low temperature in the initial stage would aid the progress of only the main process. This supposition was confirmed. Thus, the convenient method of preparation of bis-β,β'-chloroethyl ester of vinylphosphonic acid turned out to be the slow heating of a mixture of bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid and triethylamine (in molar ratio of 1:1.02) in a benzene solution. The precipitate of triethylamine hydrochloride was removed as completely as possible (see experimental part), and bis-β,β'-chloroethyl vinylphosphonate was fractionated in vacuo. The yield was about 70% of theoretical. We should note that the admixture of triethylamine hydrochloride (if this is not washed out completely) during the distillation suffers a partial decomposition and is partially drawn into the distillate. Pure bis-β,β'-chloroethyl ester of vinylphosphonic acid distills without decomposition.

The above-described method, in connection with the previously developed method of safe preparation of bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid [12], makes di-β,β'-chloroethyl vinylphosphonate a readily available substance.

## EXPERIMENTAL

The initial bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid was prepared by the previously described method [12].

Preparation of bis-β,β'-chloroethyl vinylphosphonate. (One of typical experiments.) A mixture of 1080 g of bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid, 412 g of triethylamine and 1000 ml of benzene, protected from atmospheric moisture, was stirred for 3 hrs at 30-40°, 2 hrs at 50-60° and 3 hrs at 80-85°. The resulting precipitate of triethylamine hydrochloride was filtered off on the following day and washed with benzene. Benzene was distilled from the filtrate. The residue, from which some crystals had precipitated again, was filtered, the filtrate was washed with water and fractionated at 3-4 mm. There were obtained the following fractions: 1st, with b. p. 22-135°; 2nd with b. p. 135-146°, 591 g; 3rd with b. p. 146-161°, 135 g. After repeated distillation of the second and the third fractions there was obtained 601 g of bis-β,β'-chloroethyl vinylphosphonate (yield with account being taken of recovery of the starting material was 70% of theoretical) and 80 g of unreacted bis-β,β'-chloroethyl ester of β-chloroethylphosphonic acid.

B. p. 131-132° (3 mm), 135-137° (4 mm), $n^{20}D$ 1.4787, $d_4^{20}$ 1.3233, $MR_D$ 49.91; calc. 50.13 (in the calculation we used the atomic increment values cited in [13]).

Found %: P 13.3; Cl 30.8. $C_6H_{11}O_3PCl_2$. Calculated %: P 13.3; Cl 30.5.

With a rapid running of the reaction with the same molar ratios of the components, the yields of bis-β,β'-chloroethyl vinylphosphonate dropped by 10-12%. Bis-β,β'-chloroethyl ester of vinylphosphonic acid was a colorless transparent liquid, soluble in benzene, toluene, alcohol and ether, insoluble in water.

## SUMMARY

The method of preparation of bis-β,β'-chloroethyl ester of vinylphosphonic acid in yields of about 70% of theoretical was described.

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# A NEW METHOD OF INTRODUCTION OF TRIHALOMETHYL GROUP
## INTO ORGANIC COMPOUNDS

N. N. Iarovenko and A. S. Vasil'eva

The goal of the present work was the search for a method of replacement of hydrogen in a hydroxyl group in an organic compound by a trifluoromethyl group: $ROH \rightarrow ROCF_3$. It is known that certain dyes containing the polyfluoroalkoxyl group, for example, $CF_3CH_2O$, possess interesting properties [1]. Dyes containing the trifluoromethoxyl group have been studied but little up to the present time [2].

A new method for introduction of the trihalomethyl group into organic compounds was discovered during a study of chemical properties of phenyl ester of chlorothiocarbonic acid (see also [3]). We showed that this compound is capable of readily adding two atoms of chlorine with formation of phenoxydichloromethylenesulfenyl chloride:

$$ROC{\overset{S}{\underset{Cl}{\diagup}}} \xrightarrow{Cl_2} ROCCl_2SCl$$
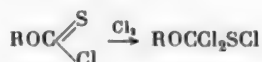
Upon further chlorination, the sulfur is completely eliminated in the form of chlorides of sulfur and there is formed trichloromethyl phenyl ether:

$$ROCCl_2SCl \xrightarrow{Cl_2} ROCCl_3$$
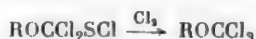
Fluorination of this ether proceeds very readily. Difluorochloromethyl phenyl ether was obtained on heating trichloromethyl phenyl ether with antimony trifluoride without a catalyst. The reaction begins after a slight heating and proceeds quietly in a usual glass flask. A deeper fluorination of trichloromethyl phenyl ether does not occur without a catalyst even at 200°, but should one add a small amount of antimony pentachloride, the spontaneously progressing exothermic fluorination to trifluoromethyl phenyl ether takes place.

$$C_6H_5OCCl_3 \xrightarrow{SbF_3} C_6H_5OCF_2Cl$$
$$C_6H_5OCF_2Cl \xrightarrow{SbF_3+SbCl_5} C_6H_5OCF_3$$
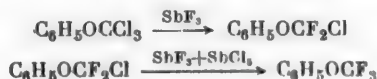
## EXPERIMENTAL

Trichloromethyl phenyl ether. 20 g of phenyl ester of chlorothiocarbonic acid was saturated with chlorine with simultaneous cooling with ice water, until the weight gain of chlorine reached 8.25 g. Then the reaction mixture was washed with water and dried with calcium chloride. The yield of phenoxydichloromethylenesulfenyl chloride was 21 g (74.5%). The substance was a yellow liquid with an odor characteristic of alkylsulfenyl chlorides. It was insoluble in water. It dissolved readily in ether and chloroform. It decomposed on attempted distillation; $d_4^{19}$ 1.4306, $n^{19}D$ 1.5690.

Found %: Cl 44.49; S 13.09. $C_7H_5OCl_3S$. Calculated %: Cl 43.80; S 13.16.

The product (8.5 g) was saturated with chlorine at 40-45° until the weight gain of chlorine reached 2.5 g. The sulfur chlorides were distilled and the trichloromethyl phenyl ether was distilled at 108-110° (16 mm). The

yield of trichloromethyl phenyl ether was 7 g (95%), $d_4^{15}$ 1.406, $n^{15}$D 1.5395. (Preparation of trichloromethyl phenyl ether from phenyl ester of chlorothiocarbonic acid may be run in one step without isolation of the intermediate substance.) The compound was a colorless liquid with an unpleasant odor. It does not dissolve in water, but is readily soluble in ether and chloroform.

Found %: C 39.45; H 2.64; Cl 49.41. $C_7H_5OCl_3$. Calculated %: C 39.81; H 2.37; Cl 50.00.

Difluorochloromethyl phenyl ether. In a glass flask there was mixed 11 g (0.062 mole) of antimony trifluoride and 13 g (0.062 mole) of trichloromethyl phenyl ether and the mixture was heated slowly to 75°. After 10-15 min following the completion of the reaction, the liquid products were distilled at the pressure of 90-100 mm, washed with dilute hydrochloric acid and, after drying with calcium chloride, again distilled at 71° (58 mm). The yield of difluorochloromethyl phenyl ether was 6 g (52%); $d_4^{18}$ 1.2748, $n^{18}$D 1.4518. The product was a colorless liquid. It was insoluble in water, but dissolved readily in the usual organic solvents.

Found %: C 47.92; H 2.84; Cl 20.49; F 21.94. $C_7H_5OF_2Cl$. Calculated %: C 47.20; H 2.81; Cl 19.90; F 21.35.

Trifluoromethyl phenyl ether. To a mixture of 5 g of antimony trifluoride with 0.5 g of antimony pentachloride there was added with stirring 3 g of difluorochloromethyl phenyl ether. After termination of heat evolution of the mixture, the liquid reaction products were distilled at atmospheric pressure, washed with water, dried with calcium chloride and redistilled. The yield of trifluoromethyl phenyl ether was 3.2 g (71%).

By an analogous method there was obtained from 17 g of antimony trifluoride mixed with 2 g of antimony pentachloride and 80 g of trichloromethyl phenyl ether, 11.1 g of trifluoromethyl phenyl ether. Yield: 53%. B. p. 104°, $d_4^{21}$ 1.2800, $n^{21}$D 1.4073.

Found %: C 51.81; H 3.16; F 35.29. $C_7H_5OF_3$. Calculated %: C 51.80; H 3.08; F 35.11.

## SUMMARY

1. A new and simple method was proposed for the introduction of a trihalomethyl group into organic compounds, the method consisting of introduction of halothiocarbonyl group into an organic molecule, with a subsequent chlorination of the latter to the trihalomethyl form.

2. Trichloromethyl, difluorochloromethyl and trifluoromethyl phenyl ethers were prepared for the first time by the above method.

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[2] M. M. Iagupol'skii and V. I. Troitskaia, J. Gen. Chem. 27, 518 (1957).*

[3] I. B. Douglass and G. H. Warner, J. Am. Chem. Soc. 78, 6070 (1956).

* Original Russian pagination. See C. B. translation.

# PREPARATION OF ESTERS OF N-TRIFLUOROMETHYLTHIOLCARBAMIC ACID

N. N. Iarovenko and S. P. Motornyi

Chemistry of fluoroalkylisocyanates began its history with the work of Hückel, who in 1946 prepared mono-, di- and trifluoromethylisocyanates [1]. After Hückel, a considerable number of new fluoroalkylisocyanates were prepared and their properties studied to some degree. Thus, for example, there were published the studies of addition of methyl alcohol and some phenols to perfluoroalkylisocyanates, reactions with water, with ammonium hydroxide, with alcoholic solution of sodium hydroxide, with acetic acid [2, 3]. Recently we discovered and described a new reaction which permits one to prepare halides of the previously unknown N-trifluoromethylcarbamic acid [4].

In light of these studies a considerable interest exists in the study of reactions of perfluoroalkylisocyanates with organic compounds, containing the sulfhydryl groups. In the present work we investigated the reactions of trifluoromethylisocyanate with methyl and phenyl mercaptans. As presupposed, perfluoroalkylisocyanates readily enter into reaction with mercaptans, forming esters of N-perfluoroalkylthiolcarbamic acids:

$$RSH \xrightarrow{CF_3NCO} CF_3NH-C\underset{SR}{\overset{O}{\lessgtr}}$$
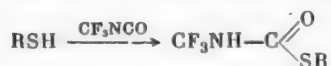
## EXPERIMENTAL

Methyl ester of N-trifluoromethylthiolcarbamic acid.   Into a glass ampule of 30 ml capacity there was placed 1.5 g of methyl mercaptan and, with cooling of the ampule with liquid nitrogen, 3.6 g of trifluoromethyl-isocyanate was condensed in it. After being sealed, the ampule was warmed to room temperature, at which an energetic reaction began. During this reaction, the ampule was periodically immersed in liquid nitrogen. After completion of the reaction, the product in the form of colorless crystals was removed from the ampule; this corresponded by analysis to methyl ester of N-trifluoromethylthiolcarbamic acid. Yield was 3.6 g (63%).

Found %: N 9.09; F 35.72; S 19.63. $C_3H_4F_3ONS$. Calculated %: N 8.80; F 35.84; S 20.12.

Phenyl ester of N-trifluoromethylthiolcarbamic acid.   Into a glass ampule of 30 ml capacity there was placed 1.7 g of thiophenol and, with cooling of the ampule with liquid nitrogen, 1.8 g of trifluoromethylisocya-nate was condensed in it. After being sealed, the ampule was warmed to room temperature at which the reaction proceeded in the course of one hour without heat evolution. Then the ampule was heated for 1 hr at 50°. After completion of the reaction the solid product was removed from the ampule. The distilled product corresponded in its analysis to the phenyl ester of N-trifluoromethylthiolcarbamic acid. The substance formed colorless crystals. M. p. 116°; sublimation temperature 140° (at 2 mm). The yield was 1.9 g (50%).

Found %: N 6.97; F 25.62; S 14.91. $C_8H_6NF_3OS$. Calculated %: N 6.63; F 25.79; S 14.48.

## SUMMARY

1. The reaction of trifluoromethylisocyanate with methyl and phenyl mercapatans was studied.

2. The corresponding esters of N-trifluoromethylthiolcarbamic acid were isolated and characterized.

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Received July 29, 1957

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[*] Original Russian pagination.  See C. B. translation.

# PROPERTIES OF HETEROORGANIC COMPOUNDS IN THE LIGHT OF
# D. I. MENDELEEV'S PERIODIC SYSTEM

## I. BOILING POINTS OF COMPOUNDS OF FLUORINE AND OTHER HALOGENS

### N. N. Iarovenko

In connection with the boiling points of organic compounds of fluorine an erroneous opinion is widespread to the effect that "fluorine exerts an effect on boiling points of organic compounds which is completely different from that expected by analogy with other halogens."[*]

Such a conclusion in respect to organofluorine compounds is totally untrue.

Fluorine, like many other elements, affects the boiling point of organic compounds in complete agreement with its position in the periodic system of the elements.

By comparison of the boiling points of analogous fluorine, chlorine and bromine organic compounds we have established that the ratio of the differences of boiling points $(t_{Cl} - t_F)/(t_{Br} - t_{Cl})$ varies within small range of limits and on the average does not differ much from 1.7 (see the table).

| $t_F$ | $t_{Cl}$ | $t_{Br}$ | $\dfrac{t_{Cl} - t_F}{t_{Br} - t_{Cl}}$ |
|---|---|---|---|
| $F_2 = -188°$ | $Cl_2 = -33.9°$ | $Br_2 = 58.7°$ | 1.66 |
| $CH_3F = -78.2$ | $CH_3Cl = -23.7$ | $CH_3Br = 4.5$ | 1.92 |
| $CH_2F_2 = -51.6$ | $CH_2Cl_2 = 41.6$ | $CH_2Br_2 = 97$ | 1.68 |
| $CHF_3 = -82.2$ | $CHCl_3 = 61.2$ | $CHBr_3 = 151.2$ | 1.59 |
| $CF_4 = -128$ | $CCl_4 = 76.8$ | $CBr_4 = 189.5$ | 1.82 |
| $C_6H_5F = 85$ | $C_6H_5Cl = 132$ | $C_6H_5Br = 156$ | 1.92 |
| $COF_2 = -83$ | $COCl_2 = 12$ | $COBr_2 = 64$ | 1.83 |

The physical meaning of this coefficient consists of the fact that it represents the result of division of the difference of atomic refractions of chlorine and fluorine by the difference of atomic refractions of bromine and chlorine.

$$\frac{AR_{Cl} - AR_F}{AR_{Br} - AR_{Cl}} = \frac{5.967 - 1.0}{8.865 - 5.967} = 1.71.$$

Assuming the variation for atomic refraction of fluorine from 0.6 to 1.35, one obtained with $AR_F = 0.6$

$$\frac{AR_{Cl} - AR_F}{AR_{Br} - AR_{Cl}} = 1.85$$

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[*] A. G. Sharpe and R. N. Haszeldine, Fluorine and Its Compounds (London-New York, 1950).

and for $AR_F = 1.35$

$$\frac{AR_{Cl} - AR_F}{AR_{Br} - AR_{Cl}} = 1.59.$$

Consequently, the replacement of one halogen by another in various compounds changes the boiling point by different amounts, but the ratio $\dfrac{t_{Cl} - t_F}{t_{Br} - t_{Cl}}$ remains almost constant and equal to $\dfrac{AR_{Cl} - AR_F}{AR_{Br} - AR_{Cl}}$.

In order to simplify the calculation of boiling points of unknown organofluorine compounds with the above formula, it is possible to construct a graph for the use of which one does not need to make any arithmetic operations.
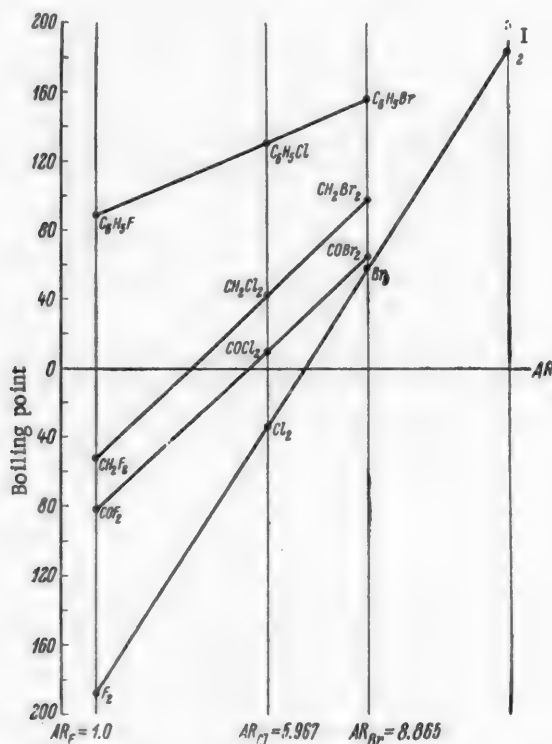


Graphic calculation of boiling points of halogen compounds.

For this purpose we draw parallel lines in respect to the temperature scale at distances equal to the atomic refractions of fluorine, chlorine and bromine and on these straight lines we lay off the known boiling points of bromine and chlorine compounds. Then, on the fluorine line one can read off the boiling points of the unknown fluorine compounds.

For an example on the above graph there is shown the calculation of the boiling points of fluorobenzene, difluoromethane and carbonyl fluoride.

It is evident that with this graph one may calculate the boiling points of not only fluorine compounds, but also those of chlorine, bromine and iodine organic compounds.

For computation of the boiling points of iodoorganic compounds it is necessary to expand the graph by one more straight line parallel to the temperature scale. The distance from this line to the temperature scale is somewhat smaller than the atomic refraction of iodine (12.9 instead of 13.9).

Below are shown the boiling points, found and calculated by the graph, for some organochlorine compounds.

## Halomethanes

$CH_3 - 23.7°$, calc. $-26°$ (from $CH_3F - 78.2°$ & $CH_2Br$  4.5°)
$CH_2Cl_2$ 41.6,  "    43 ( "   $CH_2F_2 - 51.6$ & $CH_2Br_2$ 97)
$CHCl_3$ 61.2°,  "    66 ( "   $CHF_3 - 82.2$  & $CHBr_3$  151.2)
$CCl_4$ 76.74°,  "    74 ( "     $CF_4 - 128$   & $CBr_4$   189.5)

## Haloethanes

$CH_3CH_2Cl$ 12.2°, calc. 11° (from $CH_3CH_2F - 37°$ & $CH_3CH_2Br$ 38°)
$CH_2ClCH_2Cl$ 83.5,  "    85 ( "   $CH_2FCH_2F$ 10 & $CH_2BrCH_2Br$ 129)
$CH_3CHCl_2$ 59.2,  "    60 ( "   $CH_3CHF_2 - 24.7$ & $CH_3CHBr$ 108)
$CH_2ClCHCl_2$ 114,  "    115 ( "   $CH_2FCHF_2$ 5 & $CH_2BrCHBr_2$ 188)

## Haloethylenes

$CH_2=CHCl$ $-12°$, calc. $-16°$ (from $CH_2=CHF - 72.2$ & $CH_2=CHBr$ 16°)
$CHCl=CCl_2$ 88,  "    85 ( "   $CHF=CF_2 - 51$  & $CHBr=CBr_2$ 164°)
$CCl=CCl_2$ 121,  "    117° ( "   $CF_2=CF_2 - 78.4$  &  $CBr_2=CBr_2$ 227°)

## Halopropylenes

$CF_3-CH=CHCl$ 21°, calc. 20° (from $CF_2-CH=CHF - 16°$ & $CF_3-CH=CHBr$ 40°)

## Halogenated alcohols

$CH_2ClCH_2OH$ 132°, calc. 133° (from $CH_2FCH_2OH$ 103.35° & $CH_2BrCH_2OH$ 150°)
$CHCl_2CH_2OH$ 146,  "    148 ( "   $CHF_2CH_2OH$ 96   & $CHBr_2CH_2OH$ 179)

## Halogenated aldehydes

$CCl_3COH$ 97.6°, calc. 102° (from $CF_3COH - 20°$ & $CBr_3COH$ 174°

## Halogenated acids

$CH_2ClCO_2H$ 185—187°, calc. 184° (from $CH_2FCO_2H$ 165° & $CH_2BrCO_2H$ 196°)
$CHCl_2CO_2H$ 194.4°,  "    195 ( "   $CHF_2CO_2H$ 134.2 & $CHBr_2CO_2H$ 232 with decomp.)

## Halogenated acyl halides

$CH_2ClCOCl$ 105°, calc. 113° (from $CH_2FCOF$ 52° & $CH_2BrCOBr$ 149°)
$CF_3COCl$   $-27$,  "    $-26$ ( "   $CF_3COF - 59°$ & $CF_3CO Br$   $-5$)

We also list the boiling points of some iodoorganic compounds:

$CH_3I$          43°, calc. 43° (from  $CH_3Cl$     $-23.7°$ & $CH_3Br$          4.5°)
$CF_3I$          $-22.5$,  "   $-24$ ( "   $CF_4$     $-128$ & $CF_3Br$          $-57.8$)
$C_2F_5I$         13,  "    15 ( "   $C_2F_6$      78  & $C_2F_5Cl$        $-38$)
$CF_3CH=CHI$ 70—71,  "    67 ( "   $CF_3TC=CHCl$ 21  & $CF_3CH=CHBr$  40)
$CHFlCO_2C_2H_5$ 180,  "   178 ( "   $CHF_2CO_2C_2H_5$ 99  & $CHFBrCO_2C_2H_5$ 154).

It should be noted that in some cases one may obtain an approximate notion by means of the graph concerning the boiling points of inorganic compounds as well. However, for many inorganic compounds, such as for example, hydrogen fluoride, arsenic trifluoride, cadmium fluoride, and others, there is observed a considerable deviation of the actual boiling points from those calculated by means of the graph, which fact is explained by association of the molecules of these compounds. Nevertheless even in these cases the boiling points of chlorine, bromine and iodine compounds are interconnected with atomic refractions of the halogens.

Below are shown the boiling points, both found and calculated from the graph, for some inorganic halides.

## Halides of elements of Group I

HBr      $-68.7°$, calc.$- 65°$ (from HCl  $- 85°$ & HI    $-35.7°$)
LiBr     1310,  "    1310 ( "   LiCl  1382 & LiI  1189)
NaBr     1395,  "    1370 ( "   NaCl  1413 & NaI  1300)
KCl      1415,  "    1420 ( "   K F  1505  & K Br  1380)
KI       1319,  "    1320 ( "   K F  1505  & K Br  1380)
$Cu_2Br_2$ 1345,  "    1335 ( "   $Cu_2Cl_2$ 1366 & $Cu_2I_2$ 1290)
RbCl     1385,  "    1370 ( "   RbF  1410 & RbBr 1345)

### Halides of elements of Group II

$ZnBr_2$ 650°, calc. 680°(from $ZnCl_2$ 732° & $ZnI_2$ 624°)
$CdBr_2$ 810,  "  810 ( "  $CdCl_2$ 900  & $CdI_2$ 710)
$HgBr_2$ 325,  "  320 ( "  $HgCl_2$ 301  & $HgI_2$ 349)

### Halides of elements of Group III

$BBr_3$ 90°,  calc . 95°(from $BCl_3$  12.5° & $BI_3$  210°)
$AlBr_3$ 260,  "  266 ( "  $AlCl_3$ 183  & $AlI_3$ 382)
$GaBr_3$ 278.8,  " 260 ( "  $GaCl_3$ 201  & $GaI_3$  345, sublim.)

### Halides of elements of Group IV

$SiBr_4$ 153°,  calc. 155°(from $SiCl_4$   57.6° & $SiI_4$   290°)
$SiHBr_3$ 111.8,  "  111 ( "  $SiHCl_3$ 33  & $SiHI_3$ 220)
$TiBr_4$  230,  "  230 ( "  $TiCl_4$ 135.4  & $TiI_4$  360)
$GeBr_4$ 186.5,  "  204 ( "  $GeCl_4$  83.1  & $GeI_4$  375)
$SnBr_4$ 201,  "  206 ( "  $SnCl_4$ 113.0  & $SnI_4$  340)
$SnBr_2$ 619,  "  650 ( "  $SnCl_2$ 603  & $SnI_2$  720)

### Halides of elements of Groups V and VI

$POCl_3$ 107.23°, calc. 115°(from $POF_3$ —40° & $POBr_3$ 193°)
$AsBr_3$ 221,  "  242 ( "  $AsCl_3$ 130 & $AsI_3$  400)
$NbCl_5$  240.5,  "  254 ( "  $NbF_5$ 229 & $NbBr_5$ 270)
$BiBr_3$  453,  "  470 ( "  $BiCl_3$ 447  & $BiI_3$  500)
$SeOCl_2$ 179.4,  "  183 ( "  $SeOF_2$ 124 & $SeOBr_2$ 217)

Not any less interesting is the calculation of boiling point of elemental fluorine from the boiling points of chlorine and bromine:

$$F_2 - 188°, \text{ calculated } -189° \text{ (from } Cl_2 - 33.9° \text{ and } Br_2 \ 58.7°).$$

In following communications it will be shown that by an analogous manner one is able to approximately calculate the boiling points of heteroorganic compounds of some other groups of the periodic system, as for example, the boiling points of organic compounds of sulfur from the boiling points of analogous selenium and oxygen compounds, the boiling points of organophosphorus compounds from the boiling points of analogous nitrogenous and arsenic compounds and some others.

### SUMMARY

On the basis of generalization of data on the effect of fluorine and some other elements on the boiling point of organic and inorganic compounds there was brought out a new relationship between the boiling points and atomic refraction of elements entering their compositions, and a simple method of calculation of boiling points of new compounds was suggested.

# STUDIES IN THE FIELD OF ISOQUINOLINECARBOXYLIC ACIDS

## I. PREPARATION OF 7,8-DIMETHOXYISOCARBOSTYRYL-3-CARBOXYLIC ACID, ITS ESTERS AND 7,8-DIMETHOXYISOCARBOSTYRYL

### L. I. Linevich

In the group of isoquinoline compounds one meets a great number of physiologically active substances, many of which have found an area of application as medicinal substances. The acids of this series remain an insufficiently studied and difficultly accessible group of isoquinoline compounds; only a few of its representatives have been described in the literature and the data on the biological activity of these substances are very limited. Therefore, a study of this group of isoquinoline compounds and, specifically, the development of methods for their synthesis present some interest. To the study of acids of isoquinoline series one is also drawn by the fact that among derivatives of acids, close to these in structure, of the pyridine and quinoline series, many have found an application in medicine (phthivaside, cordiamine, nupercaine).

Our problem consisted of the development of methods of preparation of a series of alkoxy substituted acids of the isoquinoline group, as well as some of their derivatives, from readily accessible raw materials — opianic acid (5,6-dimethoxy-o-aldehydobenzoic acid), which is a waste product in the production and treatment of opium alkaloids. For preparation of carboxylic acids of the isoquinoline series from opianic acid, the first step of the synthesis consists of the preparation of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid, to the development of which synthesis the present paper is devoted. The development of a convenient method, for the preparative purposes, of synthesis of this acid, as well as its esters, affords the possibility of realizing various syntheses of a whole series of isoquinoline derivatives, using these substances as starting materials.
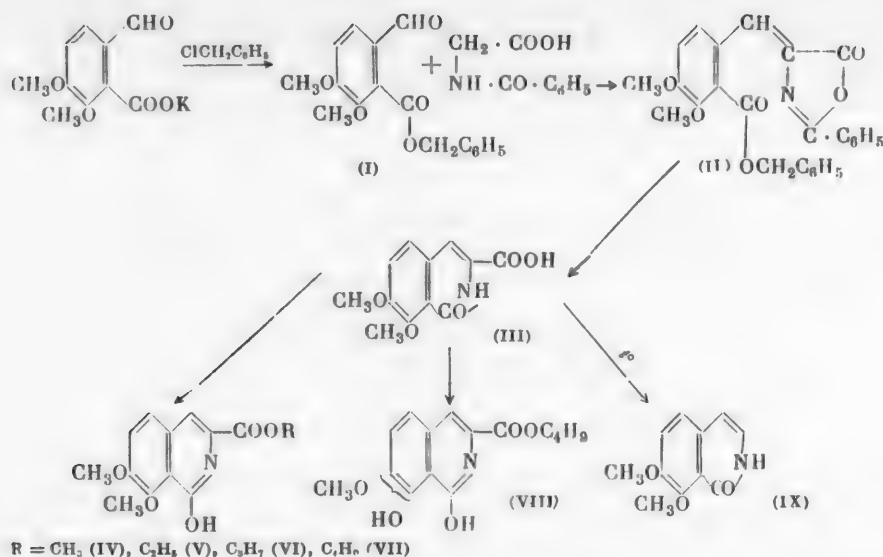
Two methods of preparation of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid are described in the literature starting with difficultly accessible methyl ester of opianic acid, but neither of these methods assures a good yield [1, 2]. By introducing several changes into Bain's method [1] we realized the synthesis of 7,8-dimethoxy-isocarbostyryl-3-carboxylic acid according to the scheme shown below with attainment of a high over-all yield of acid (III)(see diagram at top of following page).

For the starting material we used not the difficultly obtainable α-methyl ester of opianic acid, but the α-benzyl ester (I) which is readily obtained by method [3] from the potassium salt of opianic acid and benzyl chloride. Following the directions of [4] we raised the amount of benzyl chloride used in the reaction. This permitted us to raise the yield of the ester from 60% to nearly quantitative. In the condensation of α-benzyl ester (I) with hippuric acid under conditions under which Bain and co-workers obtained oxazolone from α-methyl ester of opianic acid [1], there is obtained 2-phenyl-4-(o-carboxybenzyl-m,p-dimethoxybenzal)-5-oxazolone(II) in a low yield (40-45%).* By introduction of potassium carbonate salts [5] into the reaction mixture we succeeded in raising the yield of oxazolone by a factor of two, i. e., to 85%.

The oxazolone (II) prepared by us had not been previously described; just like the oxazolone described by Bain and co-workers [1], it is readily hydrolyzed on being boiled with a solution of caustic alkali. The total yield of acid (III) in its preparation by the above-described method was about 80%, calculated on the original potassium salt of opianic acid. For characterization of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (III) and

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\* The given oxazolone was prepared by the same method by student O. O. Evdokov.

CHO
$CH_3O$ ⟶ $\xrightarrow{ClCH_2C_6H_5}$ CHO $CH_3O$ + $CH_2 \cdot COOH$ / $NH \cdot CO \cdot C_6H_5$ ⟶ $CH_3O$ ... $C \cdot C_6H_5$

$CH_3O$ COOK ... $CH_3O$ CO / $OCH_2C_6H_5$ (I) ... $CH_3O$ CO N O (II) $OCH_2C_6H_5$

$CH_3O$ —COOH / NH CO (III) $CH_3O$

$CH_3O$ —COOR / N / $CH_3O$ OH ... $CH_3O$ —$COOC_4H_9$ / N / HO OH (VIII) ... $CH_3O$ / NH CO (IX) $CH_3O$

R = $CH_3$ (IV), $C_2H_5$ (V), $C_3H_7$ (VI), $C_4H_9$ (VII)

for the further preparative work, there was prepared a series of its esters: methyl, ethyl, propyl and butyl (IV)-(VII), among which the last two had not been previously described. The esters were obtained in satisfactory yields on heating of the acid with alcohols and sulfuric acid. For preparation of the butyl ester the temperature must not be allowed to rise in the reaction mixture above 70°. At higher temperatures there occurs, besides the esterification, a cleavage of one of the methoxyl groups from the isoquinoline nucleus and there is formed the butyl ester of (7 ?)-methoxy-(8 ?)-hydroxyisocarbostyryl-3-carboxylic acid (VIII), which had not been described previously in the literature.

The reaction of decarboxylation was run with 7,8-dimethoxyisocarbostyryl-3-carboxylic acid, as the result of which there was obtained some 7,8-dimethoxyisocarbostyryl (IX) — a substance which is a convenient material for synthesis of a series of isoquinoline compounds which do not contain a carboxyl group.

## EXPERIMENTAL

Preparation of α-benzyl ester of opianic acid (I). Into a round-bottomed flask, provided with a mechanical stirrer and a reflux condenser, connected to a calcium chloride tube, there was placed 24.8 g of finely powdered anhydrous potassium salt of opianic acid • and 75 ml of benzyl chloride. With constant stirring the mixture was heated on an oil bath to 130-150° over 1.5 hr. After cooling, the reaction mixture was filtered. Benzyl chloride was distilled in vacuo from the filtrate. The residue which was the α-benzyl ester of opianic acid (I), crystallized on cooling. Its yield was 29.9 g (99.7%). M. p. 82-83° (from alcohol) (82-83° [3]).

Preparation of 2-phenyl-4-(o-carboxybenzyl-m,p-dimethoxybenzal)-5-oxazolone (II). 3 g of α-benzyl ester of opianic acid, 1.79 g of hippuric acid and 1.38 g of potassium carbonate (or the equivalent amount of potassium bicarbonate) were powdered finely and mixed. To the mixture which had been placed into a flask, there was added 3.7 ml of acetic anhydride, the flask was stoppered with a cork carrying a calcium chloride tube and a thermometer reaching the bottom of the flask, and the reaction mixture was shaken energetically. The reaction was run without any external heating. The reaction mixture turned yellow and warmed up to 40-50°; the solids dissolved completely at first, then the whole mass crystallized. The mixture was left at room temperature for 16 hrs, after which there was added 15 ml of hot water. The crystalline product was filtered off after 3 hrs and was washed with water. M. p. 158° (from glacial acetic acid and from alcohol). The yield was 7.53 g (85%).

2-Phenyl-4-(o-carboxybenzyl-m,p-dimethoxybenzal)-5-oxazolone (II) is a yellow crystalline substance, sparingly soluble in water; its solubility in the majority of organic solvents is negligible.

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• For preparation of pure potassium salt of opianic acid, the commercial opianic acid was subjected to purification by method [6] and was neutralized with potassium carbonate.

Found %: C 70.35; H 4.76; N 3.32. $C_{26}H_{21}O_6N$. Calculated %: C 70.42; H 4.78; N 3.16.

Preparation of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (III). 2-Phenyl-4-(o-carboxybenzyl-m,p-dimethoxybenzal)-5-oxazolone (4.43 g) was heated with 45 ml of 10% aqueous solution of potassium hydroxide in an apparatus for steam distillation. The hydrolysis was run with passage of steam into the apparatus, thus distilling the resulting benzyl alcohol. After termination of distillation of benzyl alcohol, the hydrolyzate was filtered and acidified with hydrochloric acid to Congo red. Upon this acidification there precipitated from the solution 7,8-dimethoxyisocarbostyryl-3-carboxylic and benzoic acids. Benzoic acid was steam distilled from this mixture (the presence of benzoic acid in the distillate was verified by a test with ferric chloride), while the 7,8-dimethoxy-isocarbostyryl-3-carboxylic acid was filtered off. The yield was 2.44 g (98%); m. p. 261° (on Macquenne block) (from glacial acetic acid), which agreed with literature data [1].

Preparation of esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (IV)-(VI). a) A mixture of 2.49 g of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid, 50 ml of anhydrous alcohol (methyl, ethyl or propyl) and 1.35 ml of sulfuric acid (d 1.84) was heated in a flask under a reflux condenser for 9 hrs on a boiling water bath. The resulting solution was poured into 150 g of a mixture of ice and water, containing 3 g of sodium carbonate. The ester which crystallized from the mixture was rapidly filtered off and washed with water until neutral to phenolphthalein. The filtrate was acidified with hydrochloric acid to Congo red and the precipitated 7,8-dimethoxyiso-carbostyryl-3-carboxylic acid was filtered off. The yield of the methyl ester (IV) was 1.70 g (65%), m. p. 195° (from methyl alcohol) (m. p. 195° [1]). The yield of the ethyl ester (V) was 1.08 g (75%), m. p. 180° (from ethyl alcohol) (m. p. 179° [1]). The yield of the propyl ester (VI) was 2.25 g (77%), m. p. 146° (from propyl alcohol).

Found %: C 61.67; H 5.81; N 4.74. $C_{15}H_{17}O_5N$. Calculated %: C 61.84; H 5.88; N 4.81.

b) Preparation of butyl ester (VII). 7,8-Dimethoxyisocarbostyryl-3-carboxylic acid (2.49 g) was dissolved with heating in 200 ml of butyl alcohol. To the solution, cooled to 60-65°, there was added 1.2 ml of sulfuric acid (d 1.84) and the mixture was heated under a reflux condenser for 24 hrs at 60-65°. The resulting solution was washed with water, 2% solution of sodium carbonate and again with water until neutral to phenolphthalein. The washed solution of the butyl ester in butyl alcohol was then dried with anhydrous sodium sulfate, after which the butyl alcohol was distilled from it in vacuo. The yield was 1.86 g (64%); m. p. 128° (from butyl alcohol).

Found %: C 62.90; H 6.09; N 4.70. $C_{16}H_{19}O_5N$. Calculated %: C 62.94; H 6.27; N 4.59.

The esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid are colorless crystalline substances. The melting points in their series drop with increase in molecular weight. The esters are soluble in organic solvents, with the higher homologs being more soluble than the lower ones; the esters are practically insoluble in water. Alcoholic solutions of the esters give a green color with ferric chloride.

Cleavage of a methoxyl radical from 7,8-dimethoxyisocarbostyryl-3-carboxylic acid during its esterification with butyl alcohol. A mixture of 2.49 g of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid, 50 ml of butyl alcohol and 1.5 ml of sulfuric acid (d 1.84) was heated in a flask with a reflux condenser, provided with a calcium chloride tube, on a boiling water bath. The solution formed after heating the mixture for 8 hrs was left overnight in a refrigerator. The crystallized substance was filtered off and washed with butyl alcohol. The product was dissolved in 20 ml of acetone, the acetone solution was filtered and poured into 40 ml of a mixture of ice and water containing 0.3 g of sodium carbonate. The (VIII) ester which crystallized thereby was filtered off and washed with water until neutral to phenolphthalein. The yield was 1.23 g (42%); m. p. 168° (from toluene).

Butyl ester of (7?)-methoxy-(8?)-hydroxyisocarbostyryl-3-carboxylic acid (VIII) was a colorless crystalline substance, soluble in most organic solvents and practically insoluble in water. It gave a green color with ferric chloride. It reacts with phosphorus oxychloride, forming a product (not isolated in the pure state) which hydrolyzes very easily to the original butyl ester of methoxyhydroxyisocarbostyryl-3-carboxylic acid.

Found %: C 62.02; H 6.00; N 4.89. M 288; active H 1.97. $C_{15}H_{17}O_5N$. Calculated %: C 61.84; H 5.88; N 4.81; M 291; active H 2.

Decarboxylation of 7,8-dimethoxycarbostyryl-3-carboxylic acid was conducted by heating this acid on a salt bath at 270-300°. The heating was extended for 1 hr after which the mass was treated several times with 1% solution of potassium carbonate with heating. The undissolved residue was filtered off. 7,8-Dimethoxyisocarbo-styryl was sublimated from the residue. The yield was 73%. M. p. 233°, corresponded to the literature data [1].

7,8-Dimethoxyisocarbostyryl (IX) is a colorless substance which is practically insoluble in the majority of organic solvents; it crystallizes well from dioxane. Its alcoholic solutions give a green color with ferric chloride.

All the experiments described above are well reproduced with larger amounts (for example, 10-15 fold) of the reagents.

## SUMMARY

1. A method for the synthesis of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid was developed (using as the basis the method of Bain and co-workers) with the over-all yield of about 80%, calculated on the original potassium salt of opianic acid.

2. Four esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid, two of which (propyl and butyl), had not previously been described in the literature, were prepared in satisfactory yields.

3. It was shown that during the esterification of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid with butyl alcohol in the presence of sulfuric acid at a temperature about 100° there occurs the cleavage of one of the methoxyl groups at the isoquinoline ring.

4. A technique of preparative synthesis of 7,8-dimethoxyisocarbostyryl was developed.

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* Original Russian pagination. See C. B. translation.

# STUDIES IN THE FIELD OF ISOQUINOLINECARBOXYLIC ACIDS

## II. PREPARATION OF 1-CHLORO SUBSTITUTED CARBOXYLIC ACID OF THE ISOQUINOLINE SERIES, ITS CHLORIDE AND ESTERS AND SOME DATA ON MOBILITY OF CHLORINE IN 1-POSITION OF THE ISOQUINOLINE NUCLEUS

### L. I. Linevich

The goal of this study was the development of synthesis of a series of trialkoxy substituted acids of the isoquinoline group and some of their derivatives from opianic acid (5,6-dimethoxy-o-aldehydobenzoic acid), which is a waste product from the production of opium alkaloids. We have already written [1] about the first steps of the synthesis, which consisted of the preparation of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (I) and its esters (II)-(V).
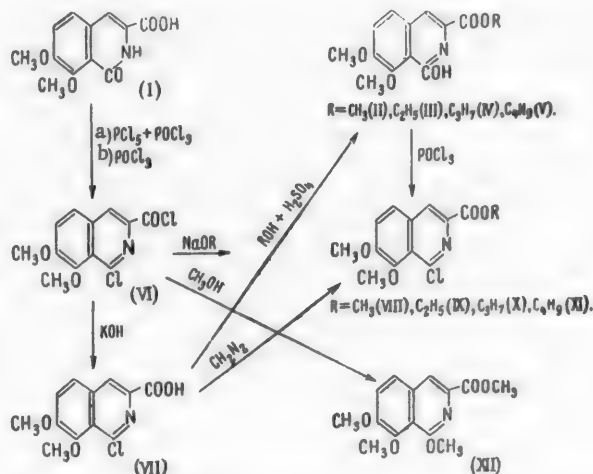


The problem in the present study consisted of the transformation of compounds of the isocarbostyryl series (I)-(V) into derivatives of 1-chloroisoquinoline (VI)-(XI), from which, by replacement of the chlorine atom by alkoxy groups, it is possible to prepare a series of trialkoxy substituted acids of the isoquinoline group and their derivatives.

We used phosphorus oxychloride and phosphorus pentachloride for the chlorinating agents. It turned out that the chlorination of derivatives of isocarbostyryl (I)-(V) proceeds under the same conditions, but that the rate of the reaction is noticeably affected by the substituent in position 3 of the isoquinoline ring. Chlorination of acid (I) was run in an organic solvent with a mixture of phosphorus pentachloride and oxychloride or by the action of excess phosphorus oxychloride. Under such conditions there takes place the formation of the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI). This acyl chloride is notable for its stability in cold water and does not dissolve in a solution of sodium carbonate. The stability of this chloride in cold water is evidently the result of its insolubility in the latter. Literature data show , for example,    a similar behavior in water of compounds close to it chemically, as for instance, the chloride of quinoline-4-carboxylic acid [2].

1-Chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VII) was prepared as the result of hydrolysis of its acyl chloride (VI) with caustic alkali. For characterization of the acid there was prepared from it by the action of diazomethane the corresponding methyl ester (VIII). The preparative synthesis of a series of esters of this acid was realized by: a) chlorination of corresponding esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (II)-(V) and by b) action of equimolar amounts of sodium alcoholates dissolved in appropriate alcohols on the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI). Thus were prepared methyl (VIII), ethyl (IX), propyl (X) and butyl (XI) esters of the chloro substituted acid. The first method of their preparation turned out to be the better one, since it assured higher yields of the esters.

We failed to prepare these esters by heating the chloro substituted acid (VII) with excess of the alcohols in the presence of sulfuric or hydrochloric acids. It turned out that under these conditions the chlorine in 1-position of the isoquinoline nucleus is rather mobile and for this reason, along with the esterification of the carboxyl group, there occurs the substitution of the chlorine by a hydroxy group, owing to which there are formed esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (II), (III). The source of the hydroxyl in this reaction is evidently the water formed in the esterification reaction.

A still greater increase of the mobility of chlorine in 1-position of the isoquinoline ring was observed in the attempt to prepare esters of the chloro substituted acid from its acyl chloride (VI) and an alcohol. During the reaction in the cold of the chloride of the chloro substituted acid (VI) with methyl alcohol there took place the formation of the methyl ester of 1,7,8-trimethoxyisoquinoline-3-carboxylic acid (XII). Thus, chlorine in 1-position of the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI) by exchanging in the cold for an alkoxyl group of an alcohol, approaches the chlorine of acyl chlorides in reactivity.

Chlorine in 1-position of the isoquinoline ring in chloro substituted acid (VII), its chloride (VI) and esters (VIII)-(XI) is rather stable in neutral and alkaline media: the acid and its esters are not decomposed on being heated with dry and wet alcohols; the chlorine in the isoquinoline nucleus of the chloro substituted acid (VII) and its chloride (VI) is not hydrolyzed when these substances are heated with a solution of alkali; during the action of equimolar amounts of sodium alcoholates in alcoholic solution on the chloride (VI), only the chlorine atom bound to the carbonyl group is exchanged for the alkoxy group, while the chlorine of the isoquinoline nucleus is not exchanged as it happens in acid medium in the absence of an alcoholate.

The increased mobility of chlorine in 1-position in the isoquinoline nucleus occurs under the influence of acids. Following facts speak of this, in addition to those listed above: during an attempt to recrystallize the chloro substituted acid (VII) from acetic acid there was obtained a substance which did not contain chlorine; on heating of not only the chloro substituted acid (VII) but also its esters (VIII) and (IX) with alcohol in the presence of sulfuric acid there were obtained esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (II) and (III).

The effect of acid on the mobility of halogen in 1-position of isoquinoline compounds was made apparent also in experiments on reduction of 1-chloro-7,8-dimethoxy-3-isoquinolyl phenyl ketone (XIII). In an attempt to reduce this chloro substituted ketone with tin and hydrochloric acid in alcoholic solution, there was obtained 7,8-dimethoxy-3-carbostyryl phenyl ketone (XIV). We succeeded in showing that its formation is the result of a hydrolytic process which proceeds in an acid medium during heating of the chloro substituted ketone (XIII) with alcohol and an inorganic acid.
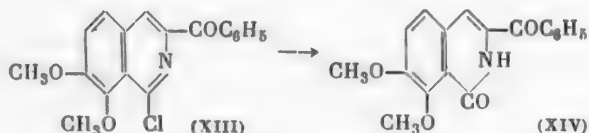


The phenomenon of increase of halogen mobility in an acid medium in nitrogenous heterocyclic compounds was discovered in 1944 by Banks [3] in the example of the reaction of substitution of chlorine in triazines by the residues of substituted amines; this reaction has been studied but little [4, 5]. In the isoquinoline series this phenomenon has not been studied at all; only in 1951 there appeared a preliminary communication stating that 1-fluoroisoquinoline does not form a hydrochloride in dilute solutions and is easily hydrolyzed by dilute acid [6].

The increase of reactivity of chlorine in the isoquinoline compounds prepared by us, as displayed in acid medium, is explained by the fact that the nitrogen in these compounds, having a pair of free electrons, adds a proton in the acid medium and therefore obtains a positive charge; owing to this the shift of the electron cloud in the isoquinoline nucleus is increased in the direction of nitrogen. Here the electron density at carbon in 1-position is particularly decreased, since this is located in $\alpha$-position in respect to the nitrogen. Therefore, a nucleophilic substitution proceeds in this location extremely readily.

Substituents in the nucleus, and specifically electronegative substituents (COCl, COOH, COOR, $COC_6H_5$) located in meta-position in respect to chlorine, should also act on the mobility of chlorine in the compounds prepared by us. The fact that the meta-located electronegative substituents do increase the activity of chlorine in an aromatic ring has been very convincingly shown by the work of V. N. Ufimtsev and M. M. Malafeeva [7]. The very high reactivity of chlorine in 1-position of isoquinoline derivatives prepared by us is evidently derived by the combination of the influence of nuclear nitrogen which increases in acid medium and the influence of the electronegative substituent in meta-position in respect to the chlorine atom.

<div align="center">EXPERIMENTAL</div>

Preparation of the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI). a) Into a round-bottomed flask provided with a reflux condenser with a calcium chloride tube there was placed 10 g of phosphorus pentachloride, 7.5 ml of phosphorus oxychloride and 200 ml of ethylene chloride dried over calcium chloride. Into the resulting solution there was added, in portions, 2.5 g of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid. The mixture was heated on a boiling water bath for 2.5 hrs, after which the solvent and phosphorus oxychloride were distilled in vacuo. The residue was recrystallized from toluene that had been distilled from sodium.

b) A mixture of 2.5 g of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid with 2.7 ml of phosphorus oxychloride was heated for 1 hr on a boiling water bath in a round-bottomed flask provided with a reflux condenser with a calcium chloride tube. After cooling, the mixture was treated with 100 g of ice and the crystallized product was filtered off and washed with water. The weight of the dry product was 2.8 g; m. p. 167°. If the resulting product is used for the preparation of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VII), there is no need to recrystallize it. No depression was observed in a mixed melting point of this substance with the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI), prepared in experiment a).

The chloride of 1-chloro-7, 8-dimethoxyisoquinoline-3-carboxylic acid (VI) was obtained in the form of light yellow crystals; the substance was insoluble in cold water and in solutions of alkali carbonates; it was not decomposed by cold water, but was hydrolyzed by solutions of caustic alkalies; it was readily soluble in organic solvents (benzene, toluene, petroleum ether); it was decomposed by alcohols both on heating and in the cold.

Preparation of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VII). The chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI) (2.86 g) was dissolved with heating in 1% solution of potassium hydroxide. The resulting solution was filtered and to the filtrate there was added 10% sulfuric acid to acid test with Congo red; the crystallized 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI) was filtered off, washed with water and recrystallized from alcohol.

Methyl ester of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VIII) was prepared by the action of an ethereal solution of diazomethane on the solution of 0.1 g of the acid in 40 ml of methyl alcohol. (The methods of preparative synthesis of this ester are described below.) The residue after the distillation of excess diazomethane and solvents from the reaction mixture was dissolved in methyl alcohol, the solution was filtered and poured into a mixture of ice with an aqueous solution of sodium carbonate. The crystallized ester was filtered off, washed with water until neutral to phenolphthalein and recrystallized from methyl alcohol.

Preparation of esters of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VIII)-(XI). a)Chlorination of esters of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (II)-(V). A mixture of 2.63 g of methyl ester of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (or the equivalent amount of ethyl, propyl, or butyl ester) and 2.73 ml of phosphorus oxychloride was heated in a round-bottomed flask, provided with a reflux condenser with a calcium chloride tube, on a water bath for 2 hrs, after which the excess phosphorus oxychloride was distilled in vacuo. For purification of the methyl (VIII), ethyl (IX) and propyl (X) esters, the residue was washed with a small amount of the corresponding alcohol, dissolved with heating in the same alcohol; the solution was filtered and poured into 450 g of a mixture of ice with water containing 0.5 g of sodium carbonate. The crystallized ester was filtered

off, washed with water until neutral to phenolphthalein and recrystallized from the corresponding alcohol. For purification of the butyl ester (XI), the residue after the distillation of phosphorus oxychloride was dissolved in dioxane and the dioxane solution was poured into a mixture of ice and water containing some sodium carbonate. The ester was recrystallized from butyl alcohol by freezing out.

b) Action of sodium alcoholate on the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI). Metallic sodium (0.23 g) was dissolved in anhydrous alcohol (40 ml of methyl, ethyl, propyl or 8 ml of butyl) and the alcoholate solution was quantitatively transferred into a flask with 2.86 g of chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI). The reaction mixture was left overnight in a tightly closed flask. The resulting solution was poured into 200 g of ice (pH of the medium in the resulting mixture should be basic). The crystallized products (VIII)-(X) were rapidly filtered off and washed with ice water until neutral to phenolphthalein. In the preparation of the butyl ester (XI), the reaction mixture after completion of the reaction was diluted with 30 ml of dioxane and the resulting solution was poured into 250 g of mixture of ice and water. The separated ester was filtered off, washed with water until neutral to phenolphthalein and recrystallized from ethyl alcohol.

The corresponding esters (VIII)-(XI) prepared by the different methods melted at the same temperature (see table) and gave no depression in mixed melting points of appropriate specimens.

1-Chloro-7,8-dimethoxyisoquinoline-3-carboxylic Acid and Its Derivatives
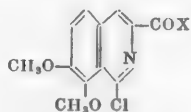


| No. of compound | X | Formula | M. p. | Yield (in %) | Elemental composition (in %) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | found | | | | calc. | | | |
| | | | | | C | H | N | Cl | C | H | N | Cl |
| (VI) | Cl | $C_{12}H_9O_3NCl_2$ | 168° | 80; 85 | 50.40 | 3.19 | 4.95 | 24.50 | 50.37 | 3.17 | 4.90 | 24.78 |
| (VII) | OH | $C_{12}H_{10}O_4NCl$ | 294 (on Mac-quenne block) | 94 | 53.74 | 3.89 | 5.31 | 13.11 | 53.84 | 3.77 | 5.23 | 13.24 |
| (VIII) | $OCH_3$ | $C_{13}H_{12}O_4NCl$ | 166 | 72; 60 | 55.40 | 4.30 | 4.95 | 12.63 | 55.42 | 4.29 | 4.97 | 12.60 |
| (IX) | $OC_2H_5$ | $C_{14}H_{14}O_4NCl$ | 106 | 71; 55 | 56.79 | 4.76 | 4.84 | 11.96 | 56.86 | 4.77 | 4.73 | 11.99 |
| (X) | $OC_3H_7$ | $C_{15}H_{16}O_4NCl$ | 102 | 62; 60 | 57.99 | 5.24 | 4.66 | 11.41 | 58.16 | 5.21 | 4.52 | 11.45 |
| (XI) | $OC_4H_9$ | $C_{16}H_{18}O_4NCl$ | 77 | 80; 75 | 59.47 | 5.65 | 4.47 | 10.86 | 59.35 | 5.60 | 4.33 | 10.95 |

The four esters of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid prepared by us (methy, ethyl, propyl, and butyl) are colorless crystalline substances. The melting points in their series are lower for the higher homologs than for the lower ones. The esters are practically insoluble in water, but they are soluble in the majority of organic solvents, the solubility being greater among the higher homologs than the lower ones.

Hydrolysis of chlorine in 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid and its esters in acid medium. a) A mixture of 0.27 g of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VII) or 0.28 g of its methyl ester (VIII), 5 ml of methyl alcohol and 0.15 ml of sulfuric acid (d 1.84) was heated on a boiling water bath for 6 hrs in a flask with a reflux condenser provided with a calcium chloride tube. The resulting solution was poured into 15 g of ice and water containing 0.3 g of sodium carbonate. The crystallized ester was filtered off, washed with water until neutral to phenolphthalein. The yield was 0.17 g (65%) of methyl ester of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (II) with m. p. 195° (from alcohol) (m. p. 195° [8, 1]). The mixed melting point with methyl ester of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid prepared by us previously by another method [1] gave no depression.

b) From 0.27 g of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VII) or 0.29 g of its ethyl ester (IX), under the same conditions by replacement of methyl alcohol by ethyl alcohol there was obtained the

ethyl ester of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid (III). Yield: 0.21 g (75%), m. p. 179°. Mixed melting point with ethyl ester of 7,8-dimethoxyisocarbostyryl-3-carboxylic acid prepared by us previously by another method [1] gave no depression.

Methanolysis of chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid. A mixture of 2.86 g of the chloride of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (VI) and 10 ml of anhydrous methyl alcohol was kept in a closed flask for 16 hrs at room temperature. The resulting solution was poured into 200 g of a mixture of ice and water containing 1.5 g of sodium carbonate. The separated crystals of methyl ester of 1,7,8-trimethoxyisoquinoline-3-carboxylic acid (XII) were filtered off and washed with water until neutral to phenolphthalein. M. p. 131° (from methyl alcohol). The ester did not contain active hydrogen. The Beilstein test and the test with ferric chloride were negative.

Found %: $CH_3O$ 44.02; M 286. $C_{14}H_{15}O_5N$. Calculated %: $CH_3O$ 44.72; M 277.

Hydrolysis of chlorine in 1-chloro-7,8-dimethoxyiso-3-quinolyl phenyl ketone (XIII) in acid medium. A mixture of 0.3 g of 1-chloro-7,8-dimethoxy-3-isoquinolyl phenyl ketone (XIII), 10 ml of methyl alcohol and 0.15 ml of sulfuric acid (d 1.84) was heated on a boiling water bath for 8 hrs in a flask with a reflux condenser. The mixture was cooled, the precipitate was filtered off, washed with alcohol, 2% solution of sodium carbonate and water until neutral to phenolphthalein. The yield was 0.15 g (50%) of 7,8-dimethoxy-3-isocarbostyryl phenyl ketone (XIV) with m. p. 199° (from alcohol) (m. p. 199° [9, 10]). The mixed melting point with 7,8-dimethoxy-3-isocarbostyryl phenyl ketone prepared by us by another method [9, 10] gave no depression.

## SUMMARY

1. 1-Chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid and its chloride were prepared.

2. A series of esters of 1-chloro-7,8-dimethoxyisoquinoline-3-carboxylic acid (methyl,ethyl, propyl, and butyl) were prepared by two methods.

3. It was shown that the mobility of chlorine in 1-position in the isoquinoline nucleus in the above compounds shows an increase in acid medium and that this chlorine is readily subjected to hydrolysis and alcoholysis.

4. It was shown that chlorine in 1-chloro-7,8-dimethoxy-3-isoquinolyl phenyl ketone is readily hydrolyzed in acid medium.

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* Original Russian pagination. See C. B. translation.

# SYNTHESIS OF AMINO ACIDS OF ALIPHATIC SERIES FROM
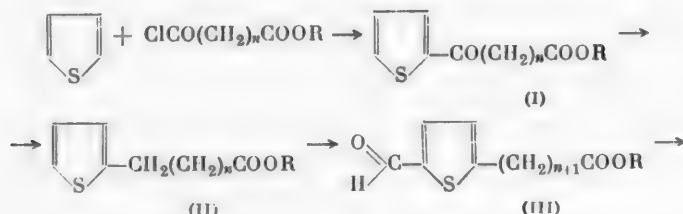# THIOPHENE DERIVATIVES

## III. SYNTHESIS OF $\omega$-AMINO ACIDS
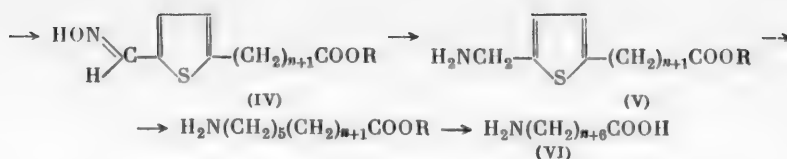
B. P. Fabrichnyi, I. F. Shalavina, and Ia. L. Gol'dfarb

$\omega$-Amino acids and the lactams formed by them have acquired a great significance in recent years mainly as the raw materials for the production of synthetic polyamide fibers. Owing to this, the interest shown by the investigators in studies of new methods of synthesis of amino acids of this type becomes understandable.

As it is known, one of the methods of preparation of lactams with 6-8 atoms of carbon is based on the use of the Beckmann rearrangement of oximes of the corresponding cyclic ketones, but this method is ill-suited for synthesis of lactams with a greater number of carbon atoms in the molecule since the starting ketones are difficult to obtain. The higher $\omega$-amino acids are formed by the action of ammonia or potassium phthalimide on the corresponding $\omega$-halogenated carboxylic acids [1, 2], by the cleavage of one molecule of water from diamides of dicarboxylic acids and by hydrogenation of the resulting amides of $\omega$-cyanocarboxylic acids, as well as from aliphatic dinitriles by reduction of one nitrile group and hydrolysis of the resulting nitriles of $\omega$-aminocarboxylic acids. Such methods do not always lead to the desired result and, for example, an attempt by M. N. Bogdanov [3] to prepare 7-aminoheptanoic acid from the dinitrile of pimelic acid ended in failure. In 1956 Treibs and Hauptmann [4] described a series of $\omega$-amino acids prepared from monoamides of dicarboxylic acids by the Hoffmann method.

In light of the above-cited data, a special interest arises in the method of preparation of amino acids from the products of telomerization of ethylene and carbon tetrachloride, a method developed at the Institute of Heteroorganic Compounds of the Academy of Sciences, USSR [5]. It should be noted, however, that the necessity of utilization of a relatively complicated apparatus makes this method inconvenient at times under the laboratory conditions. Other methods [6, 7] have only a limited significance or are based on the utilization of natural substances. One may indicate also the data related to the preparation of mixtures of various amino acids [8]. $\omega$-Amino acids with branched structure have been studied much less and they have been prepared mainly from oximes of the substituted cyclohexanones [9].

Thanks to the method of preparation of amino acids from thiophene derivatives, a method developed by us previously [10-12], the branched and the unbranched amino acids with even or odd number of atoms of carbon in the molecule have become readily accessible. Applied to $\omega$-amino acids, this is shown in the series of examples illustrated in the following scheme:

$$\rightarrow \text{HON}\!\!=\!\!\underset{H}{\overset{}{C}}\!\!-\!\!\boxed{\phantom{xx}}\!\!-\!\!(CH_2)_{n+1}COOR \rightarrow H_2NCH_2\!\!-\!\!\boxed{\phantom{xx}}\!\!-\!\!(CH_2)_{n+1}COOR \rightarrow$$

<center>(IV)                    (V)</center>

$$\rightarrow H_2N(CH_2)_5(CH_2)_{n+1}COOR \rightarrow H_2N(CH_2)_{n+6}COOH$$

<center>(VI)</center>

This method was also used by us for the synthesis of 10-amino-3-methyldecanoic acid; the substituent which creates the branching of the carbon chain was introduced by acylation of thiophene with the chloride of

$\beta$-methyl-$\gamma$-carbomethoxybutyric acid. The other possible starting materials for the preparation of aliphatic $\omega$-amino acids with branched structure are the appropriate amino acids of the thiophene series with substituents in 3- or 4-positions of the thiophene nucleus as well as amino acids with the general formula (A), where R' and R" are atoms of hydrogen or hydrocarbon residues.
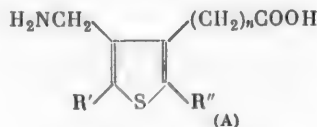
Esters of oxoacids with general formula (I), where R = $CH_3$ or $C_2H_5$, and n = 2, 3 or 4, were prepared by us by acylation of thiophene with the chlorides of $\beta$-carbomethoxypropionic, $\gamma$-carbomethoxybutyric, and $\delta$-carboethoxyvaleric acids. The yields of esters of oxoacids reached 74-86%. The carbonyl group in the synthesized esters was reduced with hydrazine hydrate by a modified Kizhner method [13] (yield: 89-97%). Since the esters are hydrolyzed under these conditions, the reaction products in these cases were the acids with structure (II) (R = H). The latter were esterified prior to formylation (yield: 87-92%; this stage is not shown in the above scheme). The formylation of esters (II) was run with N-methylformanilide in the presence of phosphorus oxychloride (yield: 77-94%), while oximation of the resulting aldehyde-esters by heating with hydroxylamine gave yields above 90%. In some cases the resulting oximes could not be crystallized and these were used for the further reaction without purification. The reduction of oximino esters to esters of amino acids was done with amalgamated aluminum under conditions described previously [12]. The use of oximino esters instead of oximino acids at the reduction step permitted us to raise considerably the yield of the products and to bring this to 88% in the case of the ester of $\epsilon$-(5-aminomethyl-2-thienyl)-hexanoic acid (V, R = $CH_3$, n = 4). In connection with the above, we shall note that the substitution for the reduction of the corresponding acetylhydrazones for the oximes of aldehyde-acids, as suggested by Decombe [14], failed to give satisfactory results. The corresponding amino acids were obtained from esters (V) by heating with a solution of barium hydroxide and neutralization with sulfuric acid. In some cases the resulting amino acids were not isolated as such, but were converted into the corresponding acetyl derivatives by the action of acetic anhydride in alkaline medium. This permitted us to raise the yield of the aliphatic amino acid since the hydrogenolysis of the acetyl derivatives proceeds with better yield than does the hydrogenolysis of esters of amino acids, reaching 83.5% for 9-acetamidononanoic acid; the hydrogenolysis was run by heating with Raney nickel in a dilute ammonia solution.

The hydrochlorides of the amino acids were obtained by heating the $\omega$-acetamido acids with dilute hydrochloric acid; the melting points of the former agreed with the data cited in the literature.

By the above technique we were able to prepare the previously known 9-aminononanoic (VI, n = 2), 10-aminodecanoic (VI, n = 3), 11-aminoundecanoic (VI, n = 4) acids, while 10-amino-3-methyldecanoic acid is being described for the first time.

An attempt to prepare the ester of aliphatic $\omega$-amino acid directly by hydrogenolysis of the oxime of aldehydo-ester (IV) without resorting to the intermediate step of reduction of the oxime to the ester of the amino acid (V) failed to give positive results in the case of 5-(3-carbethoxypropyl)-2-thiophenaldoxime.

<center>EXPERIMENTAL</center>

The esters of oxoacids of the thiophene series were synthesized by the action of chlorides of half-esters of dicarboxylic acids on thiophene in benzene medium in the presence of stannic chloride, using the previously described technique [15] into which the following changes were introduced: benzene was distilled from the solution of the condensation product and the residue was distilled in vacuo. The properties of the resulting esters of oxoacids are shown in Table 1.

TABLE 1

| Esters of oxo acids | B.p. (pressure in mm) | $n_D^{20}$ | $d_4^{20}$ | Yield (in %) | Empirical formula | C (in %) found | C (in %) calc. | H (in %) found | H (in %) calc. | S (in %) found | S (in %) calc. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Methyl ester of β-(2-thenoyl)-propionic acid,[a] (II, n = 2, R = H) | 177° (16) | 1.5467 | — | 80 | $C_9H_{10}O_3S$ | — | — | — | — | — | — |
| Methyl ester of γ-(2-thenoyl)-butyric acid (I, n = 3) | 173 (11) | 1.5577 | 1.1943 | 74 | $C_{10}H_{12}O_3S$ | 56.90, 56.87 | 56.58 | 5.78, 5.77 | 5.70 | 15.46, 14.92 | 15.10 |
| Methyl ester of β-methyl-γ-(2-thenoyl)-butyric acid,[b] (ThCOCH₂CH(CH₃)CH₂COOCH₃) | 173—174 (13) | 1.5520 | 1.1622 | 86 | $C_{11}H_{14}O_3S$ | 58.63, 58.50 | 58.38 | 6.27, 6.22 | 6.24 | 14.50, 14.30 | 14.17 |
| Ethyl ester of δ-(2-thenoyl)valeric acid,[c] (I, n = 4) | 185—186 (12) | 1.523 | 1.1328 | 83 | $C_{12}H_{16}O_3S$ | 60.02, 59.77 | 59.97 | 6.69, 6.65 | 6.71 | 13.42, 13.55 | 13.34 |

Note. a) Literature data [16]: b. p. 178° (17 mm), $n_D^{20}$ 1.5428; b) Th – 2-thenyl; c) literature data [17]: b. p. 205° (20 mm), $d_4^{25}$ 1.122, $n_D^{20}$ 1.5152.

TABLE 2

| Esters of oxo acids | B. p. (pressure in mm) | $d_4^{20}$ | $n_D^{20}$ | Yield (in %) | Empirical formula | C (in %) found | C (in %) calc. | H (in %) found | H (in %) calc. | S (in %) found | S (in %) calc. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| γ-(2-Thienyl)-butyric acid,[a] (II, n = 2, R = H) | 168° (14.5) | — | 1.5317 | 90 | $C_8H_{10}O_2S$ | | | | | | |
| Ethyl ester[b] (II, n = 2, R = C₂H₅) | 143.5—144° (20) | 1.0797 | 1.5020 | 92 | $C_{10}H_{14}O_2S$ | 60.29, 60.39 | 60.57 | 6.97, 7.15 | 7.12 | 15.90, 16.09 | 16.17 |
| δ-(2-Thienyl)-valeric acid[c] (II, n = 3, R = H) | 177 (14) m.p. 41—43° | — | — | 90 | $C_9H_{12}O_2S$ | | | | | | |
| Methyl ester (II, n = 3, R = CH₃) | 137.5—138 (14) | 1.0620 | 1.5064 | 89 | $C_{10}H_{14}O_2S$ | 60.71, 60.85 | 60.57 | 7.31, 7.15 | 7.12 | 16.05, 16.33 | 16.17 |
| ε-(2-Thienyl)-caproic acid[d] (II, n = 4, R = H) | m.p. 41—41.5° | — | — | 97 | $C_{10}H_{14}O_2S$ | | | | | | |
| Methyl ester (II, n = 4, R = CH₃) | 143.5—144 (12) | 1.0636 | 1.5032 | 87 | $C_{11}H_{16}O_2S$ | 62.28, 62.51 | 62.23 | 7.63, 7.74 | 7.60 | 15.31, 15.16 | 15.10 |
| β-Methyl-δ-(2-thienyl)-valeric acid (ThCH₂CH₂CH(CH₃)CH₂COOH) [e] | 172—173 (12) | 1.1112 | 1.5212 | 89 | $C_{10}H_{14}O_2S$ | 60.59, 60.83 | 60.57 | 7.20, 7.03 | 7.12 | 16.23, 16.01 | 16.17 |
| Methyl ester (ThCH₂CH₂CH(CH₃)CH₂COOCH₃)[e] | 141.5—142 (14.5) | 1.0641 | 1.5037 | 87 | $C_{11}H_{16}O_2S$ | 62.42, 62.53 | 62.23 | 7.57, 7.54 | 7.60 | 14.94, 15.09 | 15.10 |

Note. a) Literature data [16, 20, 21]: b. p. 167° (14 mm), $n_D^{20}$ 1.5321; b. p. 170—172° (14 mm), 130—134° (1.5 mm); b) $n_D^{25}$ D 1.5007, MR$_D$ 54.16, calc. 53.97; ester number 287.3, calc. 282.4. Constants cited by Buu-Hoï and co-workers [23] for this ester (b. p. 164—65° at 20 mm, $n_D^{25}$ D 1.5081) did not agree with those found by us. c) Literature data [22]: b. p. 178° (14 mm), m. p. 36°; d) literature data [17]: m. p. 40°; e) Th – 2-thenyl.

β-Methyl-γ-carbomethoxybutyryl chloride, necessary for the preparation of β-methyl-γ-(2-thenoyl)-butyric acid, was prepared in the following manner. β-Methylglutaric acid [18] was heated with acetic anhydride with distillation of the resulting acetic acid through a fractionating head provided for total condensation. The resulting anhydride of β-methylglutaric acid (yield: 81%) was refluxed with methanol, the excess methanol was distilled in vacuo and the residual acid methyl ester of β-methylglutaric acid (yield: 80%) yielded the corresponding chloride (yield: 95%) on being heated for 2 hrs with thionyl chloride. The method of synthesis used by us permitted us to prepare the intermediate substances and the chloride in better yields than under previously described conditions [19].

Acids (II) were prepared by reduction of the esters of oxoacids shown in Table 1, by the Kizhner method as modified by Huang-Minlon [13]. The esters of these acids were prepared by heating the acid with a saturated solution of hydrogen chloride in the appropriate alcohol. The constants of the acids and their esters are shown in Table 2.

The resulting esters (II) were converted into the corresponding substituted 2-thiophenaldehydes by the action of N-methylformanilide in the presence of phosphorus oxychloride [24]. The oximes of the substituted 2-thiophenaldehydes were prepared by the action of a slight excess of hydroxylamine on the appropriate aldehydes in dilute alcohol.

5-(γ-Carbethoxypropyl)-2-thiophenaldoxime. To a solution of hydroxylamine (from 6.95 g of hydroxylamine hydrochloride in 15 ml of water and 5.3 g of sodium carbonate in 15 ml of water) there was added 22.6 g of 5-(γ-carbethoxypropyl)-2-thiophenaldehyde, followed by alcohol until a transparent solution formed. This was refluxed for 1 hr. To the cooled solution there was added enough water to give a stable turbidity, and on cooling of the solution a colorless oil separated, which was then extracted with ether. After distillation of ether there was obtained 22.3 g (91.7%) of an oily oxime which could not be crystallized. For cleavage of the ester group, the compound was hydrolyzed by heating with dilute alkali. Acidification with hydrochloric acid yielded the oxime of 5-(γ-carboxypropyl)-2-thiophenaldehyde, which melted with decomposition at 182-184° (from dilute methanol).

Found %: C 50.92, 50.65; H 5.29, 5.18; S 14.78, 14.98. $C_9H_{11}O_3NS$. Calculated %: C 50.69; H 5.20; S 15.03.

Oximes of 5-(δ-carbomethoxybutyl)-2-thiophenaldehyde and 5-(ε-carbomethoxypentyl)-2-thiophenaldehyde were prepared as indicated above. The oxime of 5-(γ-methyl-δ-carbomethoxybutyl)-2-thiophenaldehyde was obtained in 97% yield in the form of a yellow oil. The constants of the aldehydes prepared by us, and of their oximes and other derivatives are shown in Table 3 (melting points are given for substances recrystallized from dilute alcohol).

γ-(5-Aminomethyl-2-thienyl)-butyric acid. The solution of 13.3 g of the oxime of 5-(γ-carbethoxypropyl)-2-thiophenaldehyde in a mixture of 105 ml of alcohol and 100 ml of water was added to amalgamated aluminum [25] prepared from 20 g of aluminum in granular form. The mixture was shaken for 30 hrs. The aluminum hydroxide was filtered off and washed repeatedly with alcohol. The filtrates were combined, the alcohol and part of the water were distilled in vacuo and the residue was extracted with ether. The extract was dried with magnesium sulfate and the ether was distilled. There remained 8.5 g (67.8%) of ethyl ester of γ-(5-aminomethyl-2-thienyl)-butyric acid in the form of a yellow oil. The hydrochloride of this ester, prepared by passage of dry hydrogen chloride into an ethereal solution of the ethyl ester of the amino acid, had m. p. 148-149° (from a mixture of absolute isopropyl alcohol and acetone).

Found %: C 50.02, 50.02; H 6.92, 6.89; Cl⁻ 13.11, 13.20. $C_{11}H_{18}O_2NClS$. Calculated %: C 50.08; H 6.88; Cl⁻ 13.44.

Picrate of ethyl ester of the amino acid, prepared by addition of an aqueous solution of picric acid to an aqueous solution of the hydrochloride, had m. p. 106-107° (from dilute alcohol).

Found %: C 44.99, 44.91; H 4.36, 4.40; S 7.21, 7.02. $C_{17}H_{20}O_9N_4S$. Calculated %: C 44.73; H 4.42; S 7.03.

The hydrochloride of γ-(5-aminomethyl-2-thienyl)-butyric acid was prepared by heating the ester of the amino acid with dilute hydrochloric acid followed by evaporation of the solution; the product, after reprecipitation with ether from a solution in isopropyl alcohol, had m. p. 166-167° (with decomposition).

TABLE 3

| Aldehydes and their derivatives | B. p. (pressure in mm) | M. p. | Yield (in %) | Empirical formula | C (in %) | | H (in %) | | N (in %) | | S (in %) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | found | calc. | found | calc. | found | calc. | found | calc. |
| 5-(γ-Carbethoxypropyl)-2-thio-phenaldehyde (III, n = 2)* | 187° (13) | — | 83 | $C_{11}H_{14}O_3S$ | 58.37, 58.57 | 58.38 | 6.21, 6.27 | 6.24 | — | — | — | — |
| Semicarbazone | — | 163.5—165° | — | $C_{12}H_{17}O_3N_3S$ | — | — | — | — | 14.68, 14.94 | 14.83 | — | — |
| Acetylhydrazone | — | 99—100° | — | $C_{13}H_{18}O_3N_2S$ | 55.32, 55.10 | 55.29 | 6.62, 6.55 | 6.43 | — | — | 11.28, 11.13 | 11.36 |
| 5-(δ-Carbomethoxybutyl)-2-thio-phenaldehyde (III, n = 3) | 163—165 (1.5) | 66—67 | 94 | $C_{11}H_{14}O_3S$ | 58.27, 58.41 | 58.38 | 6.17, 6.26 | 6.24 | — | — | 14.11, 14.30 | 14.17 |
| Oxime | — | 54—55 | 97 | $C_{11}H_{15}O_3NS$ | 54.70, 54.53 | 54.75 | 6.28, 6.19 | 6.27 | — | — | 13.10, 13.20 | 13.29 |
| Semicarbazone | — | 165 | — | $C_{12}H_{17}O_3N_3S$ | — | — | — | — | 14.87, 14.86 | 14.83 | — | — |
| 5-(ε-Carbomethoxypentyl)-2-thio-phenaldehyde (III, n = 4) | 195—197 (13) | 36—37 | 77 | $C_{12}H_{16}O_3S$ | 59.76, 59.68 | 59.97 | 6.61, 6.61 | 6.71 | — | — | 13.49, 13.42 | 13.34 |
| Oxime | — | 62—63 | 95 | $C_{12}H_{17}O_3NS$ | 56.10, 56.27 | 56.44 | 6.59, 6.70 | 6.71 | — | — | 12.56, 12.75 | 12.56 |
| Semicarbazone | — | 159—160 | — | $C_{13}H_{19}O_3N_3S$ | 52.67, 52.43 | 52.50 | 6.35, 6.41 | 6.44 | — | — | 10.96, 11.07 | 10.78 |
| 5-(γ-Methyl-δ-carbomethoxybutyl)-2-thiophenaldehyde ** (T—CH₂CH₂CH(CH₃)CH₂COOCH₃)*** | 160 (2) | — | 84 | $C_{12}H_{16}O_3S$ | 60.34, 60.21 | 59.97 | 6.74, 6.83 | 6.71 | — | — | 13.13, 12.90 | 13.34 |
| Semicarbazone | — | 167—168 | — | $C_{13}H_{19}O_3N_3S$ | — | — | — | — | 14.37, 14.19 | 14.13 | — | — |

* $n^{20}$D 1.5371.
** $d_4^{20}$ 1.1320, $n^{20}$D 1.5362.
*** T – 2-formyl-5-thienyl.

Found %: C 46.23, 46.36; H 6.18, 6.10; Cl⁻ 14.70, 14.78. $C_9H_{14}O_2NClS$. Calculated %: C 45.86; H 5.99; Cl⁻ 15.04.

γ-(5-Aminomethyl-2-thienyl)-butyric acid, melting with decomposition at 213-214° (from dilute acetone), was obtained by the action of silver oxide on the above hydrochloride.

Found %: C 54.17, 54.11; H 6.61, 6.66; S 16.20, 15.91. $C_9H_{13}O_2NS$. Calculated %: C 54.24; H 6.58; S 16.09.

δ-(5-Aminomethyl-2-thienyl)-valeric acid. A solution of 20.0 g of oxime of 5-(δ-carbomethoxybutyl)-2-thiophenaldehyde in 300 ml of methanol and 150 ml of water was shaken for about 40 hrs with amalgamated aluminum (from 20 g of granular aluminum). Working up of the reaction mixture gave 15.2 g of methyl ester of δ-(5-aminomethyl-2-thienyl)-valeric acid in the form of a red-brown oil (yield 80.7%). The ester was heated for 4 hrs with a solution of 18.6 g of crystalline barium hydroxide in 100 ml of water and the resulting solution was diluted with 200 ml of water and exactly neutralized with dilute sulfuric acid. The precipitate was filtered off and repeatedly washed with boiling water. By evaporation of the filtrates there was obtained 9.18 g (yield: 52%, calculated on the oxime) of the amino acid with m. p. 182-186°. After washing with alcohol and ether and recrystallization from water, the amino acid had m. p. 201-202° (with decomposition).

Found %: N 6.63, 6.56. $C_{10}H_{15}O_2NS$. Calculated %: N 6.59.

The hydrochloride of δ-(5-aminomethyl-2-thienyl)-valeric acid was prepared by treatment of the amino acid with dilute hydrochloric acid and evaporation of the solution in vacuo; the product had m. p. 156-157.5° (from isopropyl alcohol).

Found %: C 47.94, 47.84; H 6.48, 6.53; N 5.71, 5.83; Cl⁻ 14.10, 14.01. $C_{10}H_{16}O_2NClS$. Calculated %: C 48.09; H 6.46; N 5.61; Cl⁻ 14.20.

ε-(5-Aminomethyl-2-thienyl)-caproic acid was prepared by the reduction of the oxime of 5-(ε-carbomethoxypentyl)-2-thiophenaldehyde with amalgamated aluminum and hydrolysis of the resulting methyl ester of the amino acid by heating it with a solution of barium hydroxide. The yield was 69.6% (based on oxime). After purification the amino acid melted with decomposition at 185-186° (from water).

Found %: C 57.99, 57.87; H 7.45, 7.34; N 6.04, 6.01; S 13.97, 13.78. $C_{11}H_{17}O_2NS$. Calcuated %: C 58.12; H 7.54; N 6.16; S 14.11.

The hydrochloride of this amino acid had m. p. 143-144.5° (from isopropyl alcohol).

Found %: N 5.45, 5.41; Cl⁻ 13.24, 13.42. $C_{11}H_{18}O_2NClS$. Calculated %: N 5.31; Cl⁻ 13.44.

β-Methyl-δ-(5-aminomethyl-2-thienyl)-valeric acid. From 24 g of oily oxime of 5-(γ-methyl-δ-carbomethoxybutyl)-2-thiophenaldehyde there was prepared by the above-described method 20.3 g (89.5%) of unpurified methyl ester of β-methyl-δ-(5-aminomethyl-2-thienyl)-valeric acid in the form of a light yellow oil. By hydrolysis of this ester by heating with a solution of barium hydroxide there was obtained 16.7 g of crude amino acid (yield: 78%, based on the oxime). After recrystallization from dilute acetone, the amino acid melted with decomposition at 196-198°.

Found %: C 57.87, 57.82; H 7.53, 7.60; N 6.30, 6.08; S 13.98, 13.94. $C_{11}H_{17}O_2NS$. Calculated %: C 58.12; H 7.54; N 6.16; S 14.11.

The hydrochloride of this amino acid, after reprecipitation from a solution in anhydrous isopropyl alcohol with ether, had m. p. 151-152°.

Found %: C 50.04, 49.87; H 6.88, 6.80; Cl⁻ 13.19, 13.29. $C_{11}H_{18}O_2NClS$. Calculated %: C 50.08; H 6.88; Cl⁻ 13.44.

γ-(5-Acetamidomethyl-2-thienyl)-butyric acid. There was prepared 16.7 g of ethyl ester of γ-(5-aminomethyl-2-thienyl)-butyric acid by the reduction of 25.0 g of the oxime of 5-(γ-carbethoxypropyl)-2-thiophenaldehyde in 400 ml of alcohol and 250 ml of water by amalgamated aluminum (from 37.5 g of aluminum in granular form); the ester without further purification was heated for 4 hrs with 5.9 g of sodium hydroxide in 50 ml of water. The solution was evaporated to dryness in vacuo and to the residue, dissolved in 50 ml of water, there was added gradually 10 ml of acetic anhydride with ice cooling and stirring. After 1 hr the small amount of

separated and was brought into solution by addition of sodium hydroxide solution. After acidification with hydrochloric acid there precipitated a rapidly crystallizing oil. After washing with cold water and drying there was obtained 14.7 g of the acetamido acid (yield: 59% based on the oxime); m. p. 95-96° (from water).

Found %: C 54.70, 54.70; H 6.26, 6.27; S 13.46, 13.30. $C_{11}H_{15}O_3NS$. Calculated %: C 54.75; H 6.27; S 13.29.

δ-(5-Acetamidomethyl-2-thienyl)-valeric acid. From 14.6 g of oxime of 5-(δ-carbomethoxybutyl)-2-thiophenaldehyde there was prepared, by the above-cited method, 9.1 g (59% based on the oxime) of the acetamido acid; m. p. 80-81.5° (from water).

Found %: C 56.20, 56.34; H 6.64, 6.63; S 12.52, 12.62. $C_{12}H_{17}O_3NS$. Calculated %: C 56.45; H 6.71; S 12.56.

ε-(5-Acetamidomethyl-2-thienyl)-caproic acid was prepared by reduction of the oxime of 5-(ε-carbomethoxypentyl)-2-thiophenaldehyde with amalgamated aluminum, hydrolysis of the resulting methyl ester of ε-(5-aminomethyl-2-thienyl)-caproic acid with a sodium hydroxide solution and acetylation of the amino acid with acetic anhydride. The yield was 84% based on the oxime. After repeated recrystallization from water, the acetamido acid had m. p. 93-94°.

Found %: C 57.50, 57.70; H 7.02, 7.06; S 12.01, 11.98. $C_{13}H_{19}O_3NS$. Calculated %: C 57.96; H 7.11; S 11.91.

β-Methyl-δ-(5-acetamidomethyl-2-thienyl)-valeric acid was obtained in the form of an oil from the oxime of 5-(γ-methyl-δ-carbomethoxybutyl)-2-thiophenaldehyde by the above-described method in a yield of 72.5%, based on the oxime. The crystalline acetamido acid was obtained by acetylation of the purified β-methyl-δ-(5-aminomethyl-2-thienyl)-valeric acid with acetic anhydride; m. p. 64-65° (from dilute alcohol).

Found %: C 57.87, 58.09; H 7.02, 6.93; S 11.87, 11.90. $C_{13}H_{19}O_3NS$. Calculated %: C 57.96; H 7.11; S 11.91.

9-Acetamidononanoic acid. γ-(5-Acetamidomethyl-2-thienyl)-butyric acid (5.5 g) was dissolved in 200 ml of water and 30 ml of concentrated ammonia, the solution was heated to 65° and treated with about 33 g of Raney nickel with stirring. The mixture was stirred at 70-75° for 5 hrs (until the sulfur test vanished). The nickel was filtered off and washed with hot water. The combined filtrates were evaporated to dryness in vacuo on a water bath and the residue was dissolved in 50 ml of hot water and filtered from aluminum hydroxide. The filtrate, cooled with ice, was acidified to Congo red with dilute hydrochloric acid. The resulting precipitated crystals were filtered off and washed with cold water. There was obtained 4.1 g (83.5%) of crude acetamido acid with m. p. 68-72°. The pure substance melted at 71-72° (from dilute alcohol).

Found %: C 61.28, 61.24; H 9.80, 9.74. $C_{11}H_{21}O_3N$. Calculated %: C 61.36; H 9.83.

A mixed melting point of this substance with a specimen of 9-acetamidononanoic acid prepared by us * was 71-72°.

Hydrochloride of 9-aminononanoic acid was prepared from 4.6 g of 9-acetamidononanoic acid by refluxing for 10 hrs with dilute (1 : 1) hydrochloric acid. The filtrate was evaporated to dryness in vacuo and the residue was dried over phosphoric anhydride. The crude hydrochloride (4.4 g) melted at 122-125°. After recrystallization from a mixture of anhydrous isopropyl alcohol and acetone it had m. p. 132-133°. Literature data [27, 28, 4, 1]: m. p. 115°, 115-118°, 128-129°, and 130-133°.

9-Aminononanoic acid was isolated from the solution of its hydrochloride by addition of the calculated amount of sodium carbonate; m. p. 185-186° (from water). Literature data [2, 4]: m. p. 177° and 186-187°. A mixed melting point with an authentic specimen of 9-aminononanoic acid gave no depression.

10-Acetamidodecanoic acid. From 5.4 g of δ-(5-acetamidomethyl-2-thienyl)-valeric acid, after heating with 24 g of Raney nickel, there was obtained 3.5 g (72%) of crude acetamido acid with m. p. 118.5-120°. The pure substance melted at 120-121° (from dilute alcohol).

* The speciment of 9-acetamidononanoic acid was prepared from 9-aminononanoic acid obtained from R. Kh. Freidlina. Earlier, 9-acetamidononanoic acid had not been obtained in the pure state; Middleton and Barrett [26] had prepared it in a mixture with monomethylamide of sebacic acid; the mixture had m. p. 65-72°.

Found %: C 62.47, 62.47; H 10.01, 10.08; N 6.22, 6.10. $C_{12}H_{23}O_3N$. Calculated %: C 62.85; H 10.11; N 6.11.

Hydrochloride of 10-aminodecanoic acid. By heating 2.23 g of the corresponding acetamido acid with dilute hydrochloric acid for 10 hrs there was obtained 2.0 g of crude hydrochloride. The pure hydrochloride melted at 157-159° (from a mixture of anhydrous isopropyl alcohol and acetone).

Found %: N 6.46, 6.37; Cl⁻ 15.48, 15.61. $C_{10}H_{22}O_2NCl$. Calculated %: N 6.26; Cl⁻ 15.84.

10-Aminodecanoic acid was isolated from the solution of its hydrochloride by means of sodium carbonate; m. p. 185-187° (from water). Literature data [1]: m. p. 185-186°.

Found %: C 63.56, 63.51; H 11.28, 11.17; N 7.51, 7.70. $C_{10}H_{21}O_2N$. Calculated %: C 64.13; H 11.30; N 7.48.

11-Acetamidoundecanoic acid. From 5.0 g of ε-(5-acetamidomethyl-2-thienyl)-caproic acid with m. p. 89-90° there was obtained, by the action of 40 g of Raney nickel, 2.95 g (65%) of crude acetamido acid with m. p. 81-83°. After recrystallization from dilute alcohol, m. p. 83-84°.

Found %: C 63.96, 63.74; H 10.25, 10.28. $C_{13}H_{25}O_3N$. Calculated %: C 64.16; H 10.35.

Hydrochloride of 11-aminoundecanoic acid. By hydrolysis of 1.73 g of 11-acetamidoundecanoic acid with dilute hydrochloric acid 1.72 g of crude hydrochloride with m. p. 142-144°. The pure substance had m. p. 144-145° (from a mixture of isopropyl alcohol and acetone).

Found %: N 5.89, 5.87; Cl⁻ 14.47, 14.67. $C_{11}H_{24}O_2NCl$. Calculated %: N 5.89; Cl⁻ 14.91.

11-Aminoundecanoic acid was isolated from an aqueous solution of its hydrochloride by addition of sodium carbonate. M. p. 184-186° (from water). Literature data [1]: m. p. 186-187°.

Found %: C 65.77, 65.65; H 11.44, 11.35; N 7.07, 6.98. $C_{11}H_{23}O_2N$. Calculated %: C 65.63; H 11.51; N 6.96.

10-Acetamido-3-methyldecanoic acid. By the action of 100 g of Raney nickel on a solution of 14.3 g of the oily β-methyl-δ-(5-acetamidomethyl-2-thienyl)-valeric acid in 350 ml of water and 50 ml of concentrated ammonia, with the subsequent work-up, there was obtained 8.1 g (62.4%) of crude acetamido acid with m. p. 68-72°. The pure substance had m. p. 74-75° (from dilute alcohol).

Found %: C 63.92, 63.77; H 10.19, 10.20; N 6.05, 6.15. $C_{13}H_{25}O_3N$. Calculated %: C 64.16; H 10.35; N 5.76.

Hydrochloride of 10-amino-3-methyldecanoic acid. There was obtained 2.7 g of crude hydrochloride by heating 3.0 g of crude acetamido acid with 30 ml of dilute hydrochloric acid. After three recrystallizations from a mixture of isopropyl alcohol and ether there was obtained 1.15 g of the pure hydrochloride with m. p. 83-84°. This hydrochloride was readily soluble in water and alcohol.

Found %: C 55.58, 55.81; H 9.82, 9.99; Cl⁻ 15.06, 14.66. $C_{11}H_{24}O_2NCl$. Calculated %: C 55.56; H 10.17; Cl⁻ 14.91.

10-Amino-3-methyldecanoic acid was isolated from its hydrochloride (2.38 g) by the action of silver oxide. There was obtained 1.53 g of the amino acid with m. p. 174-175.5°. The pure amino acid melted at 178-179° (from alcohol) with decomposition. It was readily soluble in cold water.

Found %: C 65.10, 64.82; H 11.34, 11.37; N 6.81, 6.99. $C_{11}H_{23}O_2N$. Calculated %: C 65.63; H 11.51; N 6.96.

## SUMMARY

1. It was shown that the previous suggested method of synthesis of aliphatic amino acids from compounds of the thiophene series may be used for the preparation of aliphatic ω-amino acids with normal and branched structures.

2. By reduction of oximes of appropriate aldehyde esters of the thiophene series there were prepared esters of γ-(5-aminomethyl-2-thienyl)-butyric, δ-(5-aminomethyl-2-thienyl)-valeric, ε-(5-aminomethyl-2-thienyl)-caproic, and β-methyl-δ-(5-aminomethyl-2-thienyl)-valeric acids.

3. By hydrogenolysis of the acetyl derivatives of the above-listed amino acids of the thiophene series there were prepared: 9-acetamidononanoic, 10-acetamidodecanoic, 11-acetamidoundecanoic and 10-acetamido-3-methyldecanoic acids and from these were prepared, by a subsequent treatment, the corresponding amino acids and their hydrochlorides.

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# SYNTHESIS OF SOME ADRENALINE DERIVATIVES

## I. SYNTHESIS OF D,L-ADRENALINE AND ITS ANALOGS

### A. L. Remizov

The synthesis of some adrenaline derivatives described in this paper were undertaken with the purpose of studying their anti-inflammatory properties. Although the majority of the compounds considered below have been known for a long time, their synthesis remained rather poorly developed and the published directions often contained inaccuracies and could not be always reproduced. Therefore the additional data obtained by us and presented in this paper have a certain significance insofar as they touch upon compounds which play an extremely important role in the physiological studies.

In the scheme proposed at one time by Stolz [1] and used by us in the present work, the synthesis of adrenaline and its analogs includes the following two steps:

1) Amination of $\omega$-chloro-3,4-dihydroxyacetophenone (I) with its transformation, depending on the amine used for the reaction, into the corresponding amino ketone:
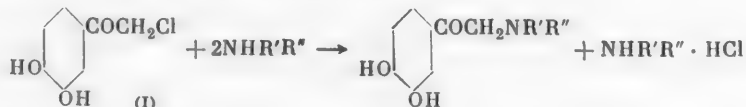


and 2) reduction of the resulting amino ketone to the corresponding secondary alcohol — D,L-adrenaline (IV) or its analog:
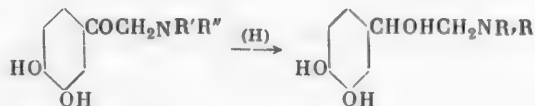


In the preparation of $\omega$-chloro-3,4-dihydroxyacetophenone (I), which is the starting material in the synthesis being discussed here, we tested three known methods[2-5] among which the preference was given to the method of Schlotta and Heller [5] in which pyrocatechol is condensed with chloroacetyl chloride. After introduction of minor changes, this method permitted us to prepare the chloro ketone with a high, and reproducible, yield.

For its transformation into $\omega$-methylamino-3,4-dihydroxyacetophenone or adrenalone (II), the dihydroxychloroacetophenone (I) was aminated by means of aqueous methylamine as described by Stolz [1] and Dakin [3] without any complications.

The $\omega$-amino-3,4-dihydroxyacetophenone — so-called noradrenalone (III) — was prepared analogously to the preparation of adrenalone. The data in the existing literature bearing on amination of dihydroxychloroacetophenone (I) with ammonia, are very brief [6]. In reproducing the directions of Stolz [1] it turned out that the process in this case proceeds less smoothly than in the preparation of adrenalone, this fact being in part connected with the concurrent intense oxidation of the reaction product. Considering this, we ran the amination under complete exclusion of air in an ammonia atmosphere, which modification raised the yield noticeably and improved the quality of the resulting noradrenalone.

Reduction of adrenalone had been until recently the most complex step in the synthesis of racemic adrenaline (IV). The best method for its realization is unquestionably the method of catalytic hydrogenation. Palladium has usually been used for the catalyst and the reaction was run in hydrochloric acid solution since the adrenalone base is practically insoluble in either water or alcohol. The conditions of hydrogenation were explored in detail in [7]. Hydrogenation of adrenalone in an alkaline solution over Raney nickel has been described also [8]. In the last paper, which had an exploratory character, the optimum reaction conditions were not fixed exactly. However, by using the data given in this paper we were able to select the conditions under which the yield of the product of hydrogenation reached 95% in individual experiments and usually was 88-90%. Thus, this step in the adrenaline synthesis may be considered at this time to be the most simple and dependable one. Hydrogenation of noradrenalone (III) to racemic $\alpha$-aminomethyl-3,4-dihydroxybenzyl alcohol (V), the so-called noradrenaline or arterenol, was also run in an alkaline medium with nickel catalyst. In this case as well the reaction proceeded well and rapidly.*
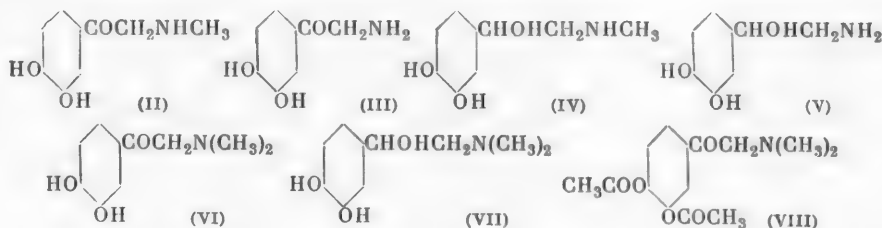


A special interest lies in the synthesis of N-methyladrenalone (VI) and D,L-N-methyladrenaline (VII). These substances, so close to the structure of noradrenalone and adrenalone and, respectively, noradrenaline and adrenaline, differ from these in physiological activity in the most radical fashion: amino ketone (VI) shows no adrenaline-like physiological activity, while amino alcohol (VII) possesses it only to a small degree [9]. They also differ in the physicochemical properties. As it is known, the bases of adrenalone and adrenaline (as well as noradrenalone and noradrenaline) do not dissolve in water and other neutral solvents and are easily isolated from the salts in the form of crystalline bases by simple addition of alkali. Their N-methyl derivatives, on the contrary, are considerably soluble in water and alcohols. Among them we succeeded in isolating only N-methyladrenalone (VI) in the form of amorphous base (until this time it was known only in the form of salts). As to the base of racemic N-methyladrenaline (VII) it was so soluble and separated from solutions so poorly that we failed to obtain it in the solid state. The absence of certain methods of preparation of N-methyladrenaline or, as it is called, metadrine, in the crystalline form forced biologists to work with specimens whose chemical individuality could be taken under much doubt. Therefore, it was important to find a method of preparation of this interesting compound in the crystalline state. After unsuccessful attempts to use the already published dubious patent data related to the base [10, 11], and the directions for preparation of metadrine hydrochloride [12] which could not be obtained in the crystalline state, we developed the conditions for its preparation with isolation of the product in the form of a stable and readily crystallizing phosphate. The raw material, as in the previous experiments, was $\omega$-chloro-3,4-dihydroxyacetophenone (I). The amination of this substance with dimethylamine, first was accomplished by S. K. Dzerzhgovskii [13] who isolated the resulting N-methyladrenalone in the form of oxalate salt which by exchange reaction with calcium chloride was transformed by him into the hydrochloride.

The directions of Dzerzhgovskii were refined by us and simplified considerably. It appeared that the oxalate prepared by that author and having m. p. 235° was not the hydrogen oxalate but the neutral salt. It also appeared that the almost completely pure hydrochloride of N-methyladrenalone may be isolated directly from the reaction mixture in 75% yield if the excess dimethylamine is preliminarily distilled off in vacuo.

It was shown that this salt exists in the form of two crystalline modifications with m. p. 236° and 212°,** the second of which had been unknown until now despite the fact that it is the more common one, although the less stable one.

Since the amorphous free base of N-methyladrenalone, isolated from the hydrochloride by us and undescribed in previous literature, could not be obtained in an analytically pure state, it was transformed for the proof of struc-

* We were the first to prepare noradrenaline under these conditions.
** Here as in the following exposition the temperature given is corrected for the exposure of the mercury column.

ture and for analysis into the diacetyl derivative (VIII) which was prepared and analyzed in the form of the base, hydrochloride and picrate.

N-Methyladrenalone could be hydrogenated in the form of the base in methanolic solution with palladium precipitated on carbon, which fact had a considerable significance from the preparative viewpoint since it considerably simplified the isolation of the hydrogenation product in the pure state. The reaction was run at room temperature with a slight excess pressure (0.2 atmos) and required 48 hrs. Upon replacement of the palladium catalyst by Raney nickel, the hydrogenation practically failed to proceed at all under these conditions, but if one added alkali to the alcoholic solution of the ketone which was being reduced, the absorption of hydrogen proceeded rapidly and quantitatively and was completely finished in 3 hrs.
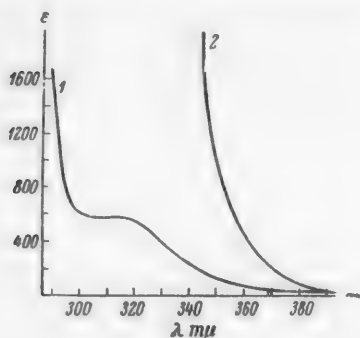


Absorption spectra: 1) of the phosphate of N-methyladrenaline, 2) of the phosphate of N-methyladrenalone.

Comparison of the data, known from the literature, about the conditions and the rates of hydrogenation of noradrenalone [6] and adrenalone [7] in acid medium (their hydrogenation in the form of free bases is impossible owing to their almost total insolubility) with the rate of this reaction as observed by us in an alkaline medium showed that in such cases there is exhibited a catalytic action of the hydroxyl ions. Thus, it is clear that an alkaline medium in hydrogenation of such compounds is necessary not only for the formation of a homogeneous solution, as might occur at first glance, but also plays an independently important role. One may allow with a considerable measure of probability that the catalytic role of hydroxyl ions is connected with the displacement of keto-enol tautomeric equilibrium toward the enolic form of the amino ketone, which is then hydrogenated at the double bond.

$$HO\langle\ \rangle COCH_2NR'R'' \underset{OH'}{\overset{OH'}{\rightleftharpoons}} HO\langle\ \rangle C=CHNR'R'' \overset{(H)}{\longrightarrow} HO\langle\ \rangle CHCH_2NR'R''$$
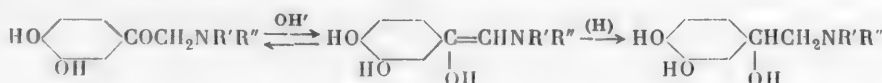
There are indications in the literature about the catalytic effect of alkali in hydrogenation of some other ketones [14].

Attempts to isolate the free base of the reaction product from the reaction mixture, obtained after hydrogenation of N-methyladrenalone, were unsuccessful. The tarry residue obtained after the removal of the solvent oxidized rapidly in air and could not be purified. However, after neutralization of it with phosphoric acid in anhydrous ethanol there was obtained in 80% yield a quite stable and readily crystallizable monosubstituted phosphate. It separated from the solution almost without loss and therefore the magnitude of the yield did not correspond to the quantitatively run hydrogenation. It was supposed that one of the reasons for the lowering of the yield may be deamination which accompanies the hydrogenation of N-methyladrenalone analogously to the previous observation of hydrogenation of some other similar amino ketones [15]. Actually, in the distillate formed after the removal of the solvent there was titrated with acid a volatile base the amount of which covered a considerable part of the unbalance of which we are speaking.

The elemental analysis of the phosphate of N-methyladrenaline prepared by us could not serve as the proof of structure of the substance since in its elemental composition this substance hardly differs from the phosphate of the original N-methyladrenalone. The latter salt was prepared specially from the base and phosphoric acid. Unfortunately, it turned out to be very similar in its properties to the metadrine phosphate and, although differing somewhat from the latter in the melting point (both salts melt unsharply with decomposition), failed to give a depression of melting point in a mixed sample. As might have been expected the substances being compared should differ greatly in the character of their light absorption in the ultraviolet region (the ketone should absorb in the region of longer waves), we determined and compared their absorption spectra which, as expected, turned out to be different, which fact proved the nonidentity of the two phosphates. As may be seen in the figure shown above, the phosphate of the hydrogenation product of N-methyladrenalone absorbs in the region of shorter waves, which fact indicates the absence of the carbonyl group in it.

# EXPERIMENTAL

$\omega$-Chloro-3,4-dihydroxyacetophenone (I) [5]. A mixture of a solution of 110 g (1 mole) of pyrocatechol in 150 ml of benzene with 124 g (1.1 mole) of chloroacetyl chloride and 9.5 g of phosphorus oxychloride was heated under a reflux condenser protected with a calcium chloride tube on a boiling water bath with mechanical stirring for 50 hrs(with interruptions). After cooling the reaction mixture to 5-10°, the resulting precipitate was filtered off, washed with benzene and was recrystallized from 150 ml of 2 N acetic acid with 1 g of carbon. The weight of the chloro ketone, dried at 110°, was 65-68 g. M. p. 172-173°.

From the benzene mother liquor after 10 days' standing in an open beaker* there separated an additional, considerable amount of the product from which, by recrystallization from 2 N acetic acid, there was obtained 40-42 g of the pure product with m. p. 171-173°. Total yield: 105-110 g (56-59%).

$\omega$-Methylamino-3,4-dihydroxyacetophenone (II). A mixture of 52 g (0.28 mole) of the chloro ketone (I), 30 ml of ethanol and 40% aqueous solution of methylamine taken in the amount which corresponded to the content of 1.4 moles of the amine,was treated according to Stolz's directions [1], after which the reaction mixture was partly neutralized (with cooling) by means of 50 ml of concentrated hydrochloric acid and was left for 30 min in an ice bath under a layer of gasoline. Then, the precipitate was filtered off, washed with 0.1% solution of aqueous sodium hydrosulfite (until the filtrate ran colorless), followed by ethanol and ether. The yield of crude product was 36-38 g (71-73%). The purification was done by transformation of the substance into the hydrochloride and the recrystallization of the latter [2]. The yield of the hydrochloride was 65% of theoretical. The free base was precipitated from the solution of the hydrochloride with aqueous ammonia at pH 9-9.5.

$\omega$-Amino-3,4-dihydroxyacetophenone (III). The reaction of dihydroxychloroacetophenone (I) and ammonia was run in a three-necked flask provided with a centrifugal stirrer with a packed gland closure, passing through a three-necked adapter set into the cork in the central neck of the flask. The side arm of the adapter was connected to a system for absorption of oxygen.** One of the side-necks of the flask carried a cork with a dropping funnel while the other one was provided with a glass tube which reached to the bottom of the flask and served for inlet of gaseous ammonia. All parts of the apparatus were connected sufficiently hermetically tightly. Into the flask was placed 60 ml of 25% aqueous ammonia and with external cooling by means of ice and salt there was introduced gaseous ammonia until complete saturation occurred. After that and with good stirring and in a weak stream of ammonia, there was added from the dropping funnel over 10-15 min a hot solution of 10 g of the chloro ketone (I) in 20 ml of methanol, while the cooling of the flask proceeded with the previous intensity. The mixing and the introduction of ammonia was continued for 6 hrs longer at room temperature, after which the reaction mixture was left overnight in an ammonia atmosphere. Then, the excess ammonia was removed by a strong current of nitrogen (finally with heating in a bath at temperature of 45-55°) and the flask contents were poured on a filter after a preliminary saturation with carbon dioxide. The precipitate was washed with ice water (until filtrate ran colorless), ethanol and ether. The crude product was purified through the hydrochloride, similarly to purification of adrenalone [2]. The yield of purified noradrenalone (free base) was 6.5-7.0 g (73-79%).

D,L-Adrenaline (IV) [8]. Hydrogenation of adrenalone was run in the apparatus commonly designed for this purpose using Raney nickel at room temperature. In order to create a slight positive pressure (0.2 atmos) in the system, the leveling bulb of the hydrogen reservoir was connected to the latter through a 2.5 m rubber tube and was suspended during the reaction some 2 m above the apparatus. The catalyst was prepared according to directions of [14] where it is called Raney nickel W-7. Into the hydrogenation vessel there was poured 50 ml of 2 N sodium hydroxide, the catalyst was added (this was prepared from 3.8 g of the alloy), the air was displaced from the system by means of hydrogen and, in a weak stream of hydrogen, there was charged 12.7 g of the adrenalone base. After 3-3.5 hrs the reaction was completed. The volume of the absorbed hydrogen exceeded by some 3-5% the calculated amount. The liquid, to which 0.1 g of sodium hydrosulfite was added immediately, was filtered off the catalyst through a glass filter into 45 ml of 4 N hydrochloric acid and the filtrate was made alkaline with ammonia solution under a layer of gasoline up to pH 9-9.5 (test with phenolphthalein paper). After 30-45 min standing in an ice bath, the precipitated adrenaline was filtered off, washed with water, ethanol and ether was dried in vacuo in the dark. Yield: 11.3-11.7 g (88-92%).

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\* With rapid distillation of the solvent (even in vacuo) there is separated a product which is badly contaminated with tar.

\** For this system we used two Drechsel flasks which were loosely filled with copper spirals moistened with saturated solution of ammonium chloride. The flasks were connected to each other by tubes which reached the bottom so that the system could work in either direction of flow.

For purification according to Savitskii [16], the adrenaline was dissolved in the minimum volume of aqueous sulfurous acid, the solution was filtered and made alkaline with ammonia under a layer of gasoline. The remaining operations in the isolation of the purified product did not differ from those described above. The yield was nearly colorless substance weighing about 11 g or 80-85% based on adrenalone.

D,L-α-Aminomethyl-3,4-dihydroxybenzyl alcohol (noradrenaline) (V). Noradrenalone (III) was hydrogenated analogously to adrenalone (see above). Absorption of hydrogen ceased after 3 hrs. After operations which were described above there was obtained noradrenaline in the form of a brownish microcrystalline powder in the yield of 76-80%.

ω-Dimethylamino-3,4-dihydroxyacetophenone (VI). A solution of 14 g of dihydroxychloroacetophenone (I) (0.075 mole) in 45 ml of hot methanol was added through a dropping funnel over 20-30 min to 0.18 mole of dimethylamine taken in the form of 30-35% solution, with stirring and cooling (temperature not above 5°). The mixture was left in a closed vessel for one day, after which it was evaporated in vacuo in a nitrogen stream to less than half the original volume for the removal of excess dimethylamine, and the residue was neutralized with ethanolic solution of hydrogen chloride (with Congo red). After 30 minutes' cooling to 0°, the precipitate was filtered off, treated in a beaker with a mixture of ethanol and acetone (1 : 2) twice, refiltered again and washed on the filter with acetone. The yield: 12.8-13.1 g (73-76%). Long prisms (from 16 parts of ethanol), with m. p. 210-212° with decomposition (after immersion of the capillary at 200°). (Literature data: m. p. 232° [11], 236° [12]). However, as shown by the analysis, the specimen prepared as described above and having m. p. 210-212°, is a pure hydrochloride of N-methyladrenalone.

Found %: Cl 15.39, 15.38. $C_{10}H_{13}O_3N \cdot HCl$. Calculated %: Cl 15.30.

After recrystallization from glacial acetic acid the substance separated in the form of prisms with m. p. 234-236° (with decomp.).

Mixed melting point of both salts was 234-236°, regardless of the composition of the mixture, which fact indicates the transition of the low melting modification into the high melting one during the heating of its mixtures with the latter.

For isolation of the base, 4.64 g of hydrochloride of N-methyladrenalone was mixed with 25 ml of dehydrated ethanol and to the mixture, heated nearly to boiling, there was added the carefully calculated amount of 1 M solution of sodium ethoxide in dehydrated ethanol. The hot solution was separated from sodium chloride by filtration and the filtrate was evaporated to dryness in vacuo in a stream of nitrogen with feeble heating. The residue was treated 4 times with 15 ml of anhydrous isopropyl alcohol at 60-65° (tar formation occurs at higher temperatures) and the resulting extract was cooled. The resulting oil transformed itself rapidly into an amorphous powder which was filtered off, washed on the filter with a small volume of cooled isopropyl alcohol and was immediately transferred into a vacuum desiccator (the product liquefies in air if it contains any solvent). The yield of dry base was 2.8-2.9 g (72-74%). From the mother liquor there was regenerated the hydrochloride with m. p. 208-210°, by neutralization with an alcoholic solution of hydrogen chloride.

The base of N-methyladrenalone is a yellowish cream powder, which is rather readily soluble in methanol, ethanol and water, especially when heated. From a hot solution in isopropyl alcohol it separates on cooling but at times in the form of a rapidly solidifying oil. It melts unsharply with decomposition at temperatures above 130°. The purified specimen with a sharp melting point was unobtainable and for this reason the elemental analysis of this substance was not run. The equivalent of the substance was determined by potentiometric titration with acid.

Found: equivalent in respect to acid 197.5. $C_6H_7O_3N(CH_3)_2$. Calculated: equivalent in respect to acid 195.2.

By neutralization of the base with hydrogen chloride or oxalic acid in an alcoholic solution there are isolated, respectively, the hydrochloride with m. p. 210-212° (decomp.) or the oxalate with m. p. 236-237°. The latter is the neutral salt, not the acid salt as indicated in the literature [13], which fact was established by analysis, by precipitation of calcium oxalate and its titration with permanganate solution.

Found %: $H_2C_2O_4$ 19.21, 18.64. $C_{10}H_{13}O_3N \cdot {}^1/_2 H_2C_2O_4$. Calculated %: $H_2C_2O_4$ 18.80.

The phosphate of N-methyladrenalone was prepared by mixing the solutions of the base and the calculated amounts of crystalline phosphoric acid in ethanol. After recrystallization from glacial acetic acid, it formed a colorless finely crystalline powder with m. p. 203-205° (decomp.).

Found %: P 10.80, 10.63. $C_{10}H_{13}O_3N \cdot H_3PO_4$. Calculated %: P 10.58.

$\omega$-Dimethylamino-3,4-diacetoxyacetophenone (VIII). To a mixture of 8 ml of anhydrous acetic acid and 5 ml of acetyl chloride, heated to 60-70°, there was added dropwise a solution of 1.95 g of the base of N-methyl-adrenalone in 8 ml of anhydrous acetic acid. After termination of the vigorous evolution of hydrogen chloride, the solution was left overnight in a closed vessel. Then the solvent was distilled as completely as possible in vacuo with mild heating. Traces of acetic acid were removed by 2-3 dissolutions of the resulting glue-like product in 15 ml of anhydrous butanol and its distillation in vacuo. After heating on a boiling water bath in good vacuum (1-2 mm), the residue solidified. It was dissolved in 5 ml of isopropyl alcohol. From this solution, after dilution with 10 ml of dry ethyl acetate, addition of a seed crystal, addition of 1-2 ml of anhydrous ether and strong cooling, there separated a crystalline precipitate, which was again recrystallized from a mixture of isopropyl alcohol and ethyl acetate. Yield: 1.4-1.5 g (44-48%). Short needles with m. p. 170-172°. The same product was obtained from the hydrochloride of N-methyladrenalone with acetyl chloride in glacial acetic acid, in the yield of 60%.

From the mother liquors after the separation and crystallization of the above hydrochloride, there was isolated an additional amount of the substance in the form of the base by evaporation of the solvent in vacuo, solution of the precipitate in a small volume of water, addition of soda solution until alkaline and rapid extraction with benzene.

Found %: Cl 11.32, 11.30. $C_{14}H_{17}O_5N \cdot HCl$. Calculated %: Cl 11.23.

The extract, dried with anhydrous sodium sulfate, was concentrated in vacuo until the beginning of crystallization and was then diluted with 4-5 volumes of petroleum ether. The yield of crystals was 0.5-0.6 g (18-21%). The total yield of the diacetyl derivative during its preparation from the hydrochloride of N-methyladrenalone was 78-84% of theoretical. The base formed colorless needles with m. p. 97-98° (from benzene with petroleum ether). It yellows rapidly in air, being transformed into the base of N-methyladrenalone.

Found %: C 60.80, 60.92; H 6.23, 6.24; N 4.98, 5.18. $C_{14}H_{17}O_5N$. Calculated %: C 60.22; H 6.13; N 5.01.

The picrate (from equimolar amounts of the base and trinitrophenol in benzene) formed bright yellow elongated hexagonal plates (from methanol) with m. p. 141.5-143°. It is readily soluble in acetone, glacial acetic acid and hot ethanol, insoluble in benzene and ether.

Found %: N 11.13, 11.04. $C_{20}H_{20}O_{12}N_4$. Calculated %: N 11.03.

N-Methyladrenaline (VII). a) Hydrogenation of N-methyladrenalone (VI) with palladium catalyst. A solution of 2 g (0.01 mole) of N-methyladrenalone base in 30 ml of methanol was shaken with 0.6 g of palladium deposited on carbon (5% Pd) [17] in hydrogen atmosphere with residual excess pressure of 0.2 atmos (see preparation of adrenaline) at room temperature. The absorption of hydrogen stopped after 48 hrs. The solution was filtered from the catalyst and was evaporated in vacuo in a stream of nitrogen to dryness in order to remove the volatile bases, the exiting vapors and gases being led through a Tishchenko flask containing 0.2 N standardized sulfuric acid solution. The dry residue was dissolved in 20 ml of anhydrous ethanol and the solution was added to 1 g of crystalline phosphoric acid dissolved in 5 ml of anhydrous ethanol. The mixture, if alkaline, was acidified to litmus with an alcoholic solution of phosphoric acid and the separated phosphate was filtered off and washed with a mixture of ethanol and acetone. Yield: 2.4 g (80%). M. p. 181-183° (with decomposition) (from glacial acetic acid with methanol and ether).

Found %: N 4.76, 4.63; P 10.65, 10.70. $C_{10}H_{15}O_3N \cdot H_3PO_4$. Calculated %: N 4.75; P 10.50.

The contents of the Tishchenko absorption flask were carefully titrated with 0.1 N sodium hydroxide with Methyl orange indicator. The content of volatile bases, calculated from the results of titration and being evidently dimethylamine, comprised 0.9 mole in one experiment, i. e., 9% of the amino ketone used in the reaction.

b) Hydrogenation of N-methyladrenalone(VI) with Raney nickel. A solution of 3.9 g (0.02 mole) of methyl-adrenalone base in 50 ml of methanol was shaken with Raney nickel, prepared from 1 g of the alloy [14], in hydro-

gen atmosphere at room temperature and 0.2 atmos of excess pressure. Over 3 hrs less than 5% of calculated volume of hydrogen was taken up. After 15 ml of 2 N solution of sodium hydroxide had been added to the solution (0.03 mole NaOH), the absorption of hydrogen proceeded rapidly and was completed in 2.5 hrs with the absorbed volume exceeding the calculated volume by 12%. After separation from the catalyst and distillation of major part of the solvent, the resulting solution residue was neutralized to litmus with an alcoholic solution of phosphoric acid and was evaporated to dryness in vacuo. The residue was treated with hot glacial acetic acid, the solution was filtered while hot from sodium phosphate and, after dilution with anhydrous ethanol and ether, and cooling, there precipitated from it a 4.02 g yield of N-methyladrenaline (68.5%).

## SUMMARY

1. The directions for preparation of adrenaline, noradrenaline and N-methyladrenaline were improved and refined.

2. The previously unknown base of N-methyladrenalone was isolated and its phosphate was prepared for the first time. The properties and the composition of the hydrochloride and the oxalate were ascertained.

3. Diacetyl derivative of N-methyladrenalone was prepared for the first time and analyzed in the form of the free base, hydrochloride and picrate.

4. Phosphate of D,L-N-methyladrenaline was prepared for the first time, this being the sole presently known crystalline preparation of this compound.

5. The catalytic influence of hydroxyl ions on the rate of hydrogenation of adrenalone and its analogs was shown. A supposition was made as to the mechanism of this effect.

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# SYNTHESIS OF THIACARBOCYANINES WITH UNSATURATED RADICALS
## AS SUBSTITUENTS

M. A. Al'perovich, I. K. Ushenko, and L. N. Tiurina

Thiacyanine dyes containing unsaturated groupings in the benzothiazole nucleus with the general formula

$$R-[CH=CH]_n \cdots \quad X^- \quad \cdots [CH=CH]_n-R$$

where $n = 1$ or $2$; $R = CH_3, C_6H_5, \gamma - C_6H_4$, or $\bigcirc_2$
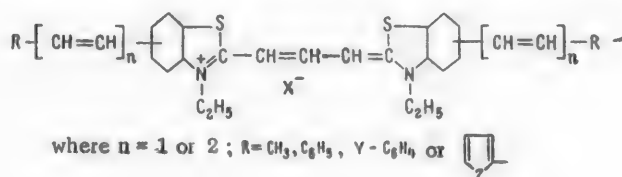
have not been described to this time. One may expect that, owing to the conjugation of unsaturated groupings with the polymethine chromophore of the thiacarbocyanine through the atom of nitrogen or sulfur [1, 2] of the thiazole ring, the conjugation chain would be lengthened as the result of which there should occur a deepening of the color of the dye. With this purpose in mind we synthesized according to the Meerwein reaction [3-11] the necessary bases by interaction of benzothiazolyldiazonium chlorides with unsaturated compounds. Heterocyclic diazo compounds had not been used in the Meerwein reaction previously. Several thiacarbocyanines containing unsaturated groupings in 6,6'-positions had been prepared by us previously [12].

In the present work we describe the synthesis of 2-methylbenzothiazoles containing various unsaturated groups in 5- or 6-positions. In the reaction of diazotized 2-methyl-5-aminobenzothiazole and 2-methyl-6-aminobenzothiazole with coumarin, cinnamic, p-methoxycinnamic, p-methylcinnamic and $\alpha$-thienylacrylic acids there were prepared seven new bases (Table 1) containing unsaturated substituents in the benzothiazole ring. Synthesis of the bases may be shown by the following scheme:
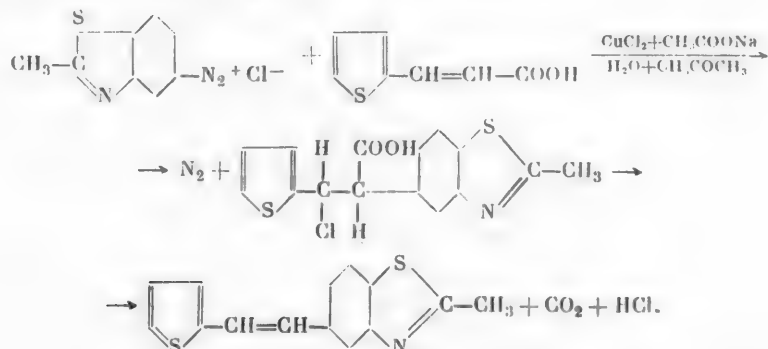


Evolution of nitrogen and carbon dioxide was observed during the synthesis. From the reaction mixture there were isolated 2-methylchlorobenzothiazoles, 2-methylbenzothiazole and chloroacetone, besides the benzothiazoles with unsaturated groups. The bases were purified by chromatography on aluminum oxide with a subsequent
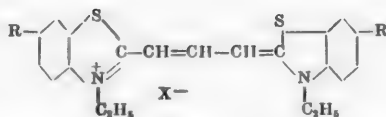
## TABLE 1

Substituted 2-Methylbenzothiazoles
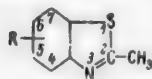


| No. of substance | R | Substituent position | Yield (in %) | Melting point |
|---|---|---|---|---|
| (I) | $C_6H_5$—CH=CH— | 5 | 20 | 138—139° |
| (II) | p -$CH_3C_6H_4$—CH=CH— | 5 | 11.7 | 128—129 |
| (III) | p -$CH_3C_6H_4$—CH=CH— | 6 | 16.8 | 155—156 |
| (IV) | p -$CH_3OC_6H_4$—CH=CH— | 5 | 14.6 | 151 |
| (V) | —CH=CH— | 5 | 9.3 | 90 |
| (VI) |  | 5 | 8.3 | 218—219 |
| (VII) |  | 6 | 5.4 | 178—179 |

## TABLE 2

Dyes
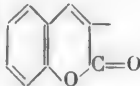


| No. of substance | R | Absorption maximum (in mμ) |
|---|---|---|
| — | H | 558 |
| — | $C_6H_5$— | 574 |
| * | $C_6H_5$—CH=CH— | 595 |
| (VIII) | p-$CH_3C_6H_4$—CH=CH— | 600 |
| * | p-$CH_3OC_6H_4$—CH=CH— | 605 |
| * | —CH=CH— | 606 |
| (IX) |  | 582 |

* Dyes which were prepared previously [12].

TABLE 3

Dyes



| No. of sub-stance | R | Absorption maximum (mμ) | | |
|---|---|---|---|---|
| | | | A | |
| | | H | CH₃ | C₂H₅ |
| — | H | 558 | 543 | 547 |
| — | C₆H₅— | 567 | 553 | 558 |
| (X) (XI) (XII) | C₆H₅—CH=CH— | 578 | 565 | 567 |
| (XIII) | p·CH₃C₆H₄—CH=CH— | 582 | — | — |
| (XIV) (XV) (XVI) | p·CH₃OC₆H₄—CH=CH— | 582 | 568 | 574 |
| (XVII) (XVIII) (XIX) | ⟨S⟩—CH=CH— | 584 | 567 | 572 |
| (XX) (XXI) | ⟨benzopyranone⟩ C=O | 570 | 556 | — |

crystallization from alcohol or ligroine. The low yield of the bases is caused by a number of side reactions: formation of 2-methylchlorobenzothiazoles, azo compounds as well as tarry products whose composition and structure were not determined by us.

By the action of alkylating agents the resulting bases were transformed into quaternary salts. The latter were introduced into a condensation with ortho esters of carboxylic acids in pyridine. The absorption maxima of the synthesized dyes, as well as of the unsubstituted thiacarbocyanine and diphenylthiacarbocyanines are shown in Tables 2 and 3.

In a comparison of the absorption maxima of the synthesized dyes with the unsubstituted thiacarbocyanine it is clear that the introduction of unsaturated groups in 5,5'- and 6,6'-positions of thiacarbocyanine strongly shifts the absorption maxima toward the longer wavelength end of the spectrum. For thiacarbocyanines with unsaturated groups in 6,6'-positions there is observed a stronger bathochromic effect than for the corresponding 5,5'-substituted thiacarbocyanines. This phenomenon may be explained evidently by the fact that the conjugation of the unsaturated groups with the polymethine chromophore is realized considerably better through a nitrogen atom of the benzothiazole nucleus than through the sulfur atom [1].

According to our data, the methyl, methoxy and methylmercapto groups introduced into the para-position of the phenyl radical in 6,6'-diphenylthiacarbocyanine do not cause a deepening of the color. However, it is clear from Tables 2 and 3 that introduction of methyl or methoxy group into the para-position of the styryl radical causes a certain shift of the absorption maximum toward the longer wavelength end of the spectrum. This shows that the presence of vinylene groups in 5,5'- or 6,6'-positions of thiacarbocyanine aids the electron displacement, which, for example, in 3,3'-diethyl-6,6'-di-(p-methoxystyryl)-thiacarbocyanine (Table 2) may be represented thus:
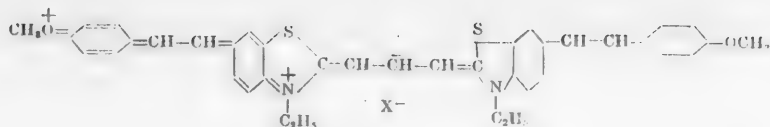
## EXPERIMENTAL

General technique of synthesis of 2-methylbenzothiazoles containing unsaturated groupings. Into a flask with a mechanical stirrer, thermometer and an outlet tube connected to a Tishchenko absorption flask containing a solution of barium hydroxide, there was placed 0.1 mole of unsaturated acid, 120-180 ml of acetone, 0.2 mole of crystalline sodium acetate and 0.03 mole of cupric chloride ($CuCl_2 \cdot 2H_2O$). The mixture was cooled with stirring to $-2°$ to $-5°$ and to it was added in small portions over 15-30 min a solution of benzothiazolyldiazonium chloride, prepared by solution of 0.1 mole of the amine in 25 ml of concentrated hydrochloric acid and 20 ml of water with subsequent diazotization with 0.11 mole of sodium nitrite in 12 ml of water. After that the mixture was stirred for 1-1.5 hr at $-2°$, after which its temperature was raised gradually until carbon dioxide began to evolve. The reaction mixture was stirred for 2-3 hrs at room temperature and was subjected to steam distillation on the following day. Acetone, chloroacetone and 2-methylchlorobenzothiazole distilled. The dark oil remaining in the distilling flask and solidifying on cooling was dissolved in chloroform and subjected to chromatography on aluminum oxide. The base was eluted with chloroform or benzene. The almost colorless zone formed by the base fluoresced with light yellow color in ultraviolet light. This zone was collected separately, the solvent was distilled off and the residue of the solvent was evaporated on a water bath. Usually a viscous yellow oil was obtained which crystallized instantly. Finally, the base was crystallized from alcohol or ligroine with use of animal charcoal.

2-Methyl-5-styrylbenzothiazole (I). 2-Methyl-5-aminobenzothiazole (16.4 g, 0.1 mole) was dissolved in 25 ml of concentrated hydrochloric acid and 20 ml of water, cooled to $-5°$ and diazotized with 7.5 g (0.11 mole) of sodium nitrite in 12 ml of water. A mixture of 14.8 g (0.1 mole) of cinnamic acid, 120 ml of acetone, 27.2 g (0.2 mole) of sodium acetate and 5.1 g (0.03 mole) of cupric chloride in 10 ml of water was cooled to $-2°$ and to this mixture there was added the diazonium chloride with energetic stirring. At 9° a slow evolution of gaseous products began and continued for one hour.

A viscous yellow oil was obtained after chromatography; it crystallized instantly. The base was recrystallized from 140 ml of methanol with the aid of animal charcoal. Yield: 2.5 g. Crystals with light yellow color; m. p. 138-139°; readily soluble in benzene, chloroform, acetone, ether, and difficultly soluble in alcohol.

Found %: S 12.52, 12.74. $C_{16}H_{13}NS$. Calculated %: S 12.71.

2-Methyl-5-(p-methylstyryl)-benzothiazole (II). Into a flask was placed 3.7 g (0.023 mole) of p-methylcinnamic acid, 60 ml of acetone, 6.2 g (0.075 mole) of sodium acetate and 1.32 g (0.0077 mole) of cupric chloride in 5 ml of water. To the cooled mixture ($-2°$) there was added with energetic stirring the diazonium chloride prepared from 3.65 g of 2-methyl-5-aminobenzothiazole, 5.7 ml of hydrochloric acid, 5 ml of water and 1.68 g of sodium nitrite in 3 ml of water. The evolution of gaseous products began at 16° and continued for 1 hr. The mixture was stirred for 1 hr at room temperature. The base was recrystallized from 80 ml of methanol. Yield: 0.68 g. Colorless crystals with m. p. 128-129°.

Found %: S 12.18, 11.92. $C_{17}H_{15}NS$. Calculated %: S 12.07.

2-Methyl-6-(p-methylstyryl)-benzothiazole (III). A mixture of 3.5 g (0.02 mole) of p-methylcinnamic acid, 60 ml of acetone, 5.8 g (0.04 mole) of sodium acetate and 1.1 g (0.0066 mole) of cupric chloride in 4 ml of water was cooled to $-2°$. To the cooled mixture there was added the diazonium salt solution prepared by diazotization of 3.46 g of 2-methyl-6-aminobenzothiazole in 5.4 ml of hydrochloric acid and 4 ml of water with 1.6 g of sodium nitrite in 3 ml of water. Evolution of carbon dioxide began at 20° and lasted for 1.5 hr. The yield, after recrystallization from methanol, 0.93 g. Colorless crystals with m. p. 155-156°.

Found %: S 11.98, 11.83. $C_{17}H_{15}NS$. Calculated %: S 12.07.

2-Methyl-5-(p-methoxystyryl)-benzothiazole (IV). 2-Methyl-5-aminobenzothiazole (16.4 g) was diazotized as indicated above. Into a flask there was placed 17.8 g (0.1 mole) of p-methoxycinnamic acid, 180 ml

of acetone, 27.2 g (0.2 mole) of sodium acetate and 5.1 g of cupric chloride in 20 ml of water. After the addition of the diazonium chloride an intense evolution of gaseous products began (at 0°) and lasted for 2 hrs. The base was crystallized from 130 ml of alcohol with the use of animal charcoal. Yield: 4.1 g. Light yellow crystals with m. p. 151°.

Found %: S 11.55, 11.77. $C_{17}H_{15}ONS$. Calculated %: S 11.39.

2-Methyl-5-(α-thienylvinyl)-benzothiazole (V). A mixture of 15.4 g (0.1 mole) of α-thienylacrylic acid, 180 ml of acetone, 27.2 g (0.2 mole) of sodium acetate and 5.1 g (0.03 mole) of cupric chloride in 20 ml of water was cooled to −2° and to the cooled mixture there was added benzothiazolyldiazonium chloride, prepared by diazotization of 16.4 g (0.1 mole) of 2-methyl-5-aminobenzothiazole. Evolution of gaseous products began at 0° and continued for 2.5 hrs. The base was crystallized from ligroine(b. p. 60-90°) for purification. Yield: 2.3 g. Colorless crystals with m. p. 90°.

Found %: S 24.93, 25.16. $C_{14}H_{11}NS_2$. Calculated %: S 24.90.

2-Methyl-5-coumarinylbenzothiazole (VI). Into a flask there was placed 7.3 g (0.05 mole) of coumarin, 50 ml of acetone, 13.6 g (0.1 mole) of cupric chloride in 5 ml of water and the mixture was cooled to −2°, after which there was added to it the diazonium chloride, prepared by diazotization of 8.2 g of 2-methyl-5-amino-benzothiazole. Evolution of nitrogen began at 15° and continued for 1.5 hr. The base was recrystallized from alcohol. Yield: 1.2 g. Colorless needles with m. p. 203-204°.

Found %: S 10.84, 11.12. $C_{17}H_{11}O_2NS$. Calculated %: S 10.92.

2-Methyl-6-coumarinylbenzothiazole (VIII) was prepared analogously to 2-methyl-5-coumarinylbenzothiazole. Evolution of nitrogen began at 12° and continued for 1 hr and 15 min. Yield: 0.75 g. Colorless crystals with m. p. 178-179°.

Found %: S 10.73, 10.92. $C_{17}H_{11}O_2NS$. Calculated %: S 10.92.

## Quaternary Salts

The quaternary salts were prepared by the usual method of heating the bases with ethyl ester of p-toluenesulfonic acid or with diethyl sulfate.

Ethyl p-toluenesulfonate of 2-methyl-5-styrylbenzothiazole. A mixture of 0.75 g (0.003 mole) of 2-methyl-5-styrylbenzothiazole and 1.2 g (0.006 mole) of ethyl ester of p-toluenesulfonic acid was heated in a flask with an air condenser on a paraffin bath at 160° (in the bath). The flask contents were dissolved in 150 ml of boiling water, the solution was extracted with benzene, boiled with animal charcoal and evaporated on a water bath. For complete removal of water, the residue was heated to 130° with stirring. Yield: 1.25 g (92.5%).

Ethiodide of 2-methyl-5-(p-methoxystyryl)-benzothiazole. 2-Methyl-5-(p-methoxystyryl)-benzothiazole (0.56 g; 0.002 mole) and 0.32 g of diethyl sulfate (0.0021 mole) were heated for 4.5 hrs at 135-140° (in the paraffin bath). 20 ml of boiling water was added to the contents of the flask. The undissolved residue (0.15 g) which turned out to be 2-methyl-5-(p-methoxystyryl)-benzothiazole, was filtered off and washed with water. The aqueous solution was concentrated to 10 ml and to it was added 1.5 g of dry potassium iodide with stirring. The light yellow crystals which precipitated were filtered off, washed with 5 ml of cold water and dried. Yield: 0.45 g (51%). Then, the ethiodide was recrystallized from alcohol. Colorless crystals with m. p. 254-255°.

Found %: I 28.30, 28.11. $C_{19}H_{20}ONSI$. Calculated %: I 29.06.

## Dyes

3,3'-Diethyl-6,6'-bis-(p-methylstyryl)-thiacarbocyanine perchlorate (VIII). A mixture of 0.052 g (0.0002 mole) of 2-methyl-6-(p-methylstyryl)-benzothiazole and 0.08 g (0.0004 mole) of ethyl ester of p-toluenesulfonic acid was heated on an oil bath for 6 hrs at 145-155°. The quaternary salt was dissolved in 1 ml of pyridine, treated with 0.3 g of ethyl orthoformate and refluxed for 20 min. The dye was precipitated with hot aqueous solution of sodium perchlorate and was recrystallized from alcohol. Small bronze-colored crystals; m. p. 229° (with decomp.). Yield: 0.04 g (30%).

Found %: N 4.06, 4.04. $C_{39}H_{37}O_4N_2S_2Cl$. Calculated %: N 4.17.

**3,3'-Diethyl-6,6'-dicoumarinylthiacarbocyanine p-toluenesulfonate (IX)** was prepared by refluxing for 15 min a mixture of 0.44 g (0.001 mole) of ethyl p-toluenesulfonate of 2-methyl-6-coumarinylbenzothiazole and 0.5 g of ethyl orthoformate in 3 ml of pyridine. The dye was precipitated with ether and was recrystallized from alcohol. Yield: 0.12 g (28%). Violet crystals with m. p. 230-232°.

Found %: S 11.94, 11.53. $C_{46}H_{36}O_7N_2S_3$. Calculated %: S 11.63.

**3,3'-Diethyl-5,5'-distyrylthiacarbocyanine p-toluenesulfonate (X).** A mixture of 0.45 g (0.001 mole) of ethyl p-toluenesulfonate of 2-methyl-5-styrylbenzothiazole, 0.5 g (0.003 mole) of ethyl orthoformate and 3 ml of pyridine was refluxed for 50 min. The dye was precipitated with ether and was recrystallized from alcohol. Yield: 0.13 g (34.6%). Violet crystals with m. p. 257-260°.

Found %: S 13.32, 13.09. $C_{44}H_{40}O_3N_2S_3$. Calculated %: S 13.54.

**3,3'-Diethyl-5,5'-distyryl-9-methylthiacarbocyanine iodide (XI).** 2-Methyl-5-styrylbenzothiazole (0.25 g, 0.001 mole) and 0.16 g of diethyl sulfate (0.0105 mole) were heated for 2 hrs at 125-130°. To the resulting quaternary salt there was added 0.32 g of ethyl orthoacetate, 2 ml of pyridine and 0.05 g of acetic anhydride and the mixture was refluxed for 15 min. The dye was precipitated with ether, dissolved in alcohol, treated with an aqueous solution of potassium iodide and recrystallized from alcohol. Yield: 0.06 g (16.8%). Violet crystals with m. p. 273-274°.

Found %: I 17.75, 17.80. $C_{38}H_{35}N_2S_2I$. Calculated %: I 17.86.

**3,3',9-Triethyl-5,5'-distyrylthiacarbocyanine iodide (XII)** was prepared analogously by heating 0.25 g (0.001 mole) of 2-methyl-5-styrylbenzothiazole and 0.16 g of diethyl sulfate for 3 hrs at 130-140°. To the quaternary salt there was added 0.26 g of ethyl orthopropionate, 2 ml of pyridine and 0.05 g of acetic anhydride and the mixture was refluxed for 15 min. Yield: 0.08 g (22%). Violet crystals with m. p. 264-265°.

Found %: I 17.32, 17.29. $C_{39}H_{37}N_2S_2I$. Calculated %: I 17.52.

**3,3'-Diethyl-5,5'-bis-(p-methylstyryl)-thiacarbocyanine ethyl sulfate (XIII).** A mixture of 0.26 g (0.001 mole) of 2-methyl-5-(p-methylstyryl)-benzothiazole and 0.16 g of diethyl sulfate was heated for 3 hrs at 130-135°. To the resulting solid mass there was added 3 ml of pyridine, 0.5 g of ethyl orthoformate and the mixture was refluxed for 20 min. The resulting crystalline precipitate was filtered off and recrystallized from alcohol. Green needles with metallic sheen; m. p. 292-293°. Yield: 0.21 g (58%).

Found %: S 12.94, 12.84. $C_{41}H_{42}O_4N_2S_3$. Calculated %: S 13.28.

**3,3'-Diethyl-5,5'-bis-(p-methoxystyryl)-thiacarbocyanine bromide (XIV)** was prepared analogously by heating 0.28 g (0.001 mole) of 2-methyl-5-(p-methoxystyryl)-benzothiazole and 0.16 g of diethyl sulfate 3 hrs at 130-135°. To the resulting quaternary salt there was added 0.5 g of ethyl orthoformate, and 3 ml of pyridine and the mixture was refluxed for 40 min. The dye was precipitated with ether and was dissolved in 160 ml of alcohol. The resulting precipitate was filtered off, washed with alcohol and with ether. Yield: 0.21 g (54%); m. p. 280-281°.

A solution of 0.1 g of the dye in 1:1 alcohol-pyridine mixture was heated to boiling and was precipitated with a hot aqueous solution of potassium bromide. After recrystallization from alcohol, the yield was 0.06 g. Dark green plates with m. p. 235-236°.

Found %: Br 11.34, 11.50. $C_{39}H_{37}O_2N_2S_2Br$. Calculated %: Br 11.28.

**3,3'-Diethyl-5,5'-bis-(p-methoxystyryl)-9-methylthiacarbocyanine iodide (XV).** A mixture of 0.28 g of 2-methyl-5-(p-methoxystyryl)-benzothiazole and 0.16 g of diethyl sulfate was heated for 3 hrs at 130-135°. To the solid brown mass there was added 0.32 g of ethyl orthoacetate, 2 ml of pyridine and 0.05 g of acetic anhydride and the mixture was refluxed for 40 min. Yield: 0.12 g (30%); m. p. 189-190°. Then the dye was dissolved in a mixture of pyridine and alcohol and was precipitated with potassium iodide. Yield: 0.05 g; m. p. 244-245°. Small crystals with a bronze sheen.

Found %: I 16.64, 16.41. $C_{40}H_{39}O_2N_2S_2I$. Calculated %: I 16.49.

**3,3',9-Triethyl-5,5'-bis-(p-methoxystyryl)-thiacarbocyanine ethyl sulfate (XVI)** was prepared analogously by heating 0.28 g of 2-methyl-5-(p-methoxystyryl)-benzothiazole and 0.16 g of diethyl sulfate for 3.5 hrs at 130-135°. To the resulting solid mass there was added 2 ml of pyridine, 0.26 g of ethyl orthopropionate and 0.05 g of

acetic anhydride and the mixture was refluxed for 40 min. The dye was precipitated with ether and was recrystallized from alcohol. Yield: 0.07 g (17.2%). Violet crystals with m. p. 252-255°.

Found %: S 12.14, 11.85. $C_{43}H_{46}O_6N_2S_3$. Calculated %: S 12.26.

3,3'-Diethyl-5,5'-bis-($\alpha$-thienylvinyl)-thiacarbocyanine p-toluenesulfonate (XVII). Ethyl p-toluenesulfonate (0.46 g) of 2-methyl-5-($\alpha$-thienylvinyl)-benzothiazole, 0.5 g of ethyl orthoformate and 3 ml of pyridine were refluxed for 40 min. The dye was precipitated with ether and was recrystallized from alcohol. Yield: 0.18 g; m. p. 220° (with decomp.). Small crystals of dark green color.

Found %: S 20.94, 20.97. $C_{40}H_{36}O_3N_2S_5$. Calculated %: S 21.25.

3,3'-Diethyl-5,5'-bis-($\alpha$-thienylvinyl)-9-methylthiacarbocyanine iodide (XVIII). A mixture of 0.26 g of 2-methyl-5-($\alpha$-thienylvinyl)-benzothiazole and 0.16 g of diethyl sulfate was heated for 3 hrs at 130-135°. To the solid mass there was added 2 ml of pyridine, 0.32 g of ethyl orthoacetate and 0.05 g of acetic anhydride and the mixture was refluxed for 40 min. The resulting precipitate of the dye was filtered off and washed with alcohol and ether. Yield: 0.15 g (29%). Violet crystals with m. p. 292-293°. The ethyl sulfate was converted into the iodide and this was recrystallized from alcohol. Yield: 0.08 g. Crystals with dark green color; m. p. 227-228°.

Found %: I 17.54, 17.64. $C_{34}H_{31}N_2S_4I$. Calculated %: I 17.59.

3,3',9-Triethyl-5,5'-bis-($\alpha$-thienylvinyl)-thiacarbocyanine iodide (XIX) was prepared by heating a mixture of 0.26 g of the base and 0.16 g of diethyl sulfate for 3.5 hrs at 130-135°. To the quaternary salt there was added 0.26 g of ethyl orthopropionate, 2 ml of pyridine and 0.05 g of acetic anhydride and the mixture was refluxed for 50 min. The dye was precipitated with ether, dissolved in 100 ml of alcohol, treated with aqueous solution of potassium iodide and recrystallized from alcohol. Yield: 0.09 g. Crystals with bronze colors; m.p. 208-209°.

Found %: I 16.95, 16.92. $C_{35}H_{33}N_2S_4I$. Calculated %: I 17.25.

3,3'-Diethyl-5,5'-dicoumarinylthiacarbocyanine p-toluenesulfonate (XX). A mixture of 0.49 g of ethyl p-toluenesulfonate of 2-methyl-5-coumarinylbenzothiazole, 0.5 g of ethyl orthoformate and 3 ml of pyridine was refluxed for 30 min. The resulting precipitate of the dye was filtered off and recrystallized from alcohol. Yield: 0.13 g (31%). Violet crystals with m. p. 255-257°.

Found %: S 10.87, 10.78. $C_{46}H_{36}O_7N_2S_3$. Calculated %: S 11.63.

3,3'-Diethyl-5,5'-dicoumarinyl-9-methylthiacarbocyanine ethyl sulfate (XXI) was prepared by heating a mixture of 0.29 g of 2-methyl-5-coumarinylbenzothiazole and 0.16 g of diethyl sulfate for 1 hr at 160-170°. To the solid mass there was added 0.32 g of ethyl orthoacetate, 2 ml of pyridine and 0.05 g of acetic anhydride and the mixture was refluxed for 20 min. The dye was precipitated with ether and was recrystallized from alcohol. Yield: 0.06 g. Green crystals with metallic sheen; m. p. 272-273°.

Found %: S 11.84, 11.92. $C_{42}H_{36}O_8N_2S_3$. Calculated %: S 12.10.

## SUMMARY

1. Seven new derivatives of benzothiazole, containing unsaturated groups in 5- or 6- positions, were prepared by the reaction of arylacrylic acids or coumarin with the diazotized 2-methyl-5-amino- or 2-methyl-6-aminobenzothiazoles.

2. Several quaternary salts were prepared by heating the bases with alkylating agents.

3. Fourteen thiacarbocyanines, containing unsaturated groups in 5- or 6-positions, were prepared by condensation of the quaternary salts with ortho esters of carboxylic acids in pyridine.

4. It was shown that the introduction of unsaturated groups into 5,5'- or 6,6'-positions of the thiacarbocyanine molecule produces a strong bathochromic effect.

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# LIQUID PHASE OXIDATION OF ALKYLAROMATIC HYDROCARBONS WITH ATMOSPHERIC OXYGEN

## OXIDATION OF p-CYMENE AND p-SEC-BUTYLTOLUENE

### V. V. Fedorova and P. G. Sergeev

According to some data [1, 2] the action of oxygen in autoxidation of p-cymene is directed to the primary $\alpha$-carbon. A hydroperoxide of p-cymene was isolated which corresponded to formula (I) [2] but no characterization of this hydroperoxide was given.



$$CH_2OOH \qquad\qquad CH_3$$

$$CH_3-CH-CH_3 \qquad CH_3-\overset{|}{\underset{OOH}{C}}-CH_3$$

$$(I) \qquad\qquad (II)$$
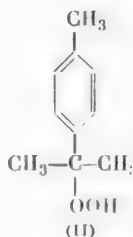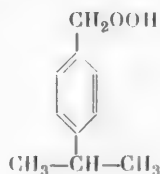
On the other hand, it was found [3] that in the oxidation of p-cymene in emulsion with aqueous alkali the sole primary oxidation product is a hydroperoxide which contains active oxygen at the tertiary $\alpha$-carbon atom (II). The hydroperoxide of such structure was also obtained later [4] in the homogeneous liquid phase oxidation of p-cymene with a catalyst at 95°. However, according to other authors [5, 6], oxidation of p-cymene proceeds at both the primary and the tertiary $\alpha$-carbon atoms.

In 1953 we set up some experiments for the study of oxidation of p-cymene by atmospheric oxygen in the presence of a small amount of a catalyst which was soluble in the hydrocarbon, as well as in an aqueous alkaline emulsion, in order to isolate the resulting hydroperoxides and to establish their structures. In both cases there was isolated from the oxidized hydrocarbon only the tertiary hydroperoxide (II), whose structure was established by the reaction with sulfuric acid. Along with the hydroperoxide there were found among the oxidation products in oxidized p-cymene some cumyl aldehyde and p-methylacetophenone, while after oxidation in the homogeneous medium there was also isolated some cumic acid. In the emulsion oxidation, the aqueous layer, which contained both the emulsifier and the acidic products of reaction, was not examined by us.

The results obtained by us give basis for considering that in the oxidation of p-cymene the oxygen reacts at both the primary and the tertiary $\alpha$-carbon atoms of the side chains, forming hydroperoxides of two types. The direction of the reaction is not changed by change in the method of oxidation. At the end of our investigation there was published a paper [7] in which it was found that the relative activity of the methyl and the isopropyl groups in the p-cymene relative to oxygen and in emulsion and in photochemical oxidation at 85° stands in the ratio of 1 : 3.5.

p-sec-Butyltoluene, analogous to p-cymene, has one primary and one tertiary $\alpha$-carbon atom, which are capable of being oxidized. No literature data exist concerning the oxidation of this hydrocarbon.

We ran the oxidation of p-sec-butyltoluene in homogeneous medium under the same conditions as in the oxidation of p-cymene. In the reaction mixture after the oxidation there were found, in addition to the hydroperoxide, some p-sec-butylbenzaldehyde and p-methylacetophenone, which fact speaks for oxidation of p-sec-butyltoluene yielding the hydroperoxides of both types (III) and (IV). The reaction scheme may be represented as:
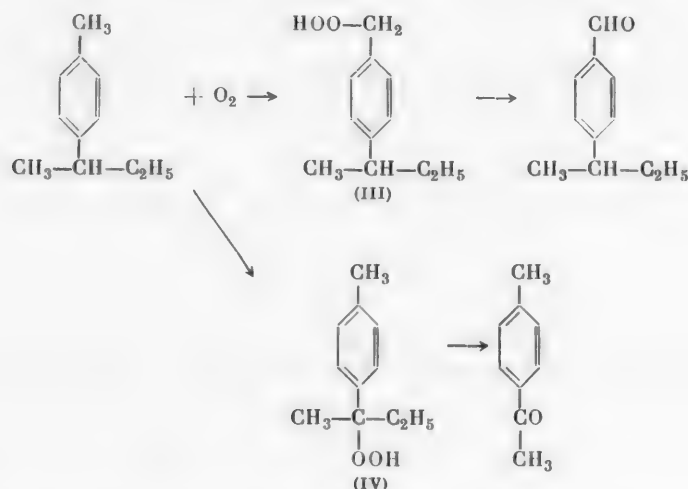


The hydroperoxide of p-sec-butyltoluene, isolated by us, corresponded to formula (IV), which was confirmed by the decomposition of this hydroperoxide in the presence of sulfuric acid into p-cresol and methyl ethyl ketone.

## EXPERIMENTAL

Oxidation of p-cymene. Prior to oxidation p-cymene was washed with sulfuric acid (d 1.84), water, sodium hydroxide solution and water, and after drying was carefully fractionated.

B. p. 30-30.5° at 2 mm, $n^{20}$D 1.4906, $d_4^{20}$ 0.8579. According to data of [8]: b. p. 177.25° at 760 mm, $n^{20}$D 1.4909, $d_4^{20}$ 0.8573.

The oxidation was run in a cylindrical flask with a widened upper portion, provided with a reflux condenser (connected to a trap), a thermometer, stirrer and a capillary tube for air inlet.

In the homogeneous oxidation experiments, p-cymene was charged into the flask along with manganese resinate (5 mg per mole) and a few drops of 97% isopropylbenzene hydroperoxide as an initiator of oxidation. The temperature of p-cymene was raised to 110°, after which dry air was introduced into it at the rate of 8-10 liters/hr per mole of material. The amount of absorbed oxygen amounted to 0.5-0.6 liters/hr per mole during the initial 4 hrs of oxidation. The content of the hydroperoxide determined iodometrically grew at the rate of 2.7-3% per hour,* which remained constant for 6-7 hrs, then began to decline. After 12 hrs the reaction mixture had accumulated up to 24% of the hydroperoxide.

For the emulsion oxidation there was charged into the reactor 50 ml of p-cymene, 100 ml of 1.3% soda solution, 0.15 g of sodium stearate and a few drops of isopropylbenzene hydroperoxide. The oxidation was run at 95°. The amount of hydroperoxide after 18 hrs was 5.8%.

Isolation of cumyl aldehyde. The oxidized p-cymene (1.38 g) which contained 14.11% of the hydroperoxide, was dissolved in ethyl alcohol and shaken energetically for 4 hrs with excess 40% solution of sodium bisulfite in order to destroy the hydroperoxide.

The aldehyde which was present gave a water soluble compound with the excess sodium bisulfite; the aqueous layer was separated while the hydrocarbon layer was repeatedly treated with sodium bisulfite for a com-

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* The calculation was made conditionally based on monohydroperoxide.

plete removal of the aldehyde. The treatment of the aqueous solution of the bisulfite compound of the aldehyde with 2,4-dinitrophenylhydrazine solution in 2 N hydrochloric acid led to the isolation of a precipitate of a 2,4-dinitrophenylhydrazone. M. p. 236-238° (from xylene). According to data [9]: m. p. 241°.

Found %: C 56.91, 56.92; H 5.17, 5.56; N 16.37. $C_{16}H_{16}O_4N_4$. Calculated %: C 58.53; H 4.94; N 17.06.

A certain divergence from the literature data in the melting point and the analyses, in respect to the carbon and nitrogen content, can be explained probably by the incomplete separation of cumyl aldehyde from the ketone present in the reaction mixture.

Isolation of p-methylacetophenone. From the hydrocarbon layer remaining after the isolation of cumyl aldehyde in the form of its bisulfite compound, there was isolated the p-methylacetophenone in the form of its 2,4-dinitrophenylhydrazone. M. p. 252-253.8°. Mixed melting point gave no depression with an authentic sample.

In the emulsion method of oxidation of p-cymene, there was isolated from the hydrocarbon layer by the same method as above a quantity of the 2,4-dinitrophenylhydrazones of cumyl aldehyde and p-methylacetophenone.

Isolation of cumic acid. p-Cymene (76 g) oxidized in the presence of manganese resinate and containing 14.11% of hydroperoxide, was treated with 5% solution of sodium bicarbonate. After evaporation and acidification of the sodium carbonate extract, there was obtained 0.82 g of cumic acid. M. p. 115° (from water). According to data [9]: m. p. 115-116°.

Isolation of hydroperoxide. Oxidized p-cymene (76 g) containing 14.11% of hydroperoxide was first washed successively with solutions of 5% sodium bicarbonate and 0.5% sodium hydroxide in order to remove acids and phenols, after which it was treated with 15 ml of 5% sodium hydroxide with cooling.

The oxidized p-cymene, after having been washed with water and with alkali, was subjected to a vacuum distillation (6 mm) for the removal of unreacted p-cymene. The residue after the distillation (13.24 g), containing 49.2% of hydroperoxide, was diluted with benzene and treated with 7 ml of 25% sodium hydroxide with cooling. The precipitate of the sodium salt of the hydroperoxide, which formed after standing, was separated, dissolved in water and the solution was saturated with carbon dioxide. The resulting oil was extracted with ether, after the distillation of which there remained 4.91 g of a viscous liquid containing by analysis 75.96% of monohydroperoxide. This liquid was again treated with 25% sodium hydroxide with isolation of the sodium salt of hydroperoxide and isolation of a still more concentrated hydroperoxide. The latter specimen was distilled in vacuo at residual pressure of $10^{-3}$ mm, which led to the isolation of 1.67 g of a fraction which formed a faintly colored liquid with a penetrating odor.

B. p. 35-38° at 0.001 mm, $n^{20}D$ 1.5199, $d_4^{20}$ 1.0369. $MR_D$ 48.72; calc. 48.82. Found %: C 71.66, 71.68; H 8.79, 8.74; active O 9.11. $C_{10}H_{14}O_2$. Calculated %: C 72.25; H 8.49; active O 9.62.

A sample (1.278 g) of the hydroperoxide was dissolved in 5 ml of ether and this solution was decomposed by a mixture of 5 ml of ether and 10 drops of sulfuric acid (d 1.84). The temperature of the mixture during the decomposition did not rise over 40°. The decomposed mass was neutralized with potassium carbonate and to it was added 10% solution of sodium hydroxide in order to bind p-cresol. Acetone was separated from the cresolate solution by steam distillation and its content in the distillate was determined by the reaction with a solution of hydroxylamine hydrochloride. p-Cresol, remaining in the flask after the distillation of acetone, was determined iodometrically. There was found in the analysis of the decomposed mass (in % of theoretical content): p-cresol 100, acetone 86. p-Cresol was identified in the form of p-cresoxyacetic acid; m. p. 135.5°. According to data [10]: m. p. 136°.

Found %: C 65.34, 65.62; H 6.2, 6.6. $C_9H_{10}O_3$. Calculated %: C 65.04; H 6.06.

Acetone was identified in the form of its 2,4-dinitrophenylhydrazone. M. p. 124-125.3° (from alcohol). According to data [11]: m. p. 126°.

Oxidation of p-sec-butyltoluene. The starting material, p-sec-butyltoluene, was prepared by alkylation of toluene with 2-butene in the presence of 5% of aluminum chloride at 42°. The p-sec-butyltoluene which was isolated by distillation through a laboratory fractionating column, was washed with sulfuric acid (d 1.84), then neutralized with alkali and was again washed with water. It was carefully fractionated after drying.

B. p. 56.5-57° at 4.5 mm, $d_4^{20}$ 0.865, $n^{20}D$ 1.4934. According to data [12]: b. p. 193-194° at 760 mm, $d_4^{20}$ 0.8665, $n^{20}D$ 1.4938.

After oxidation of the resulting butyltoluene with potassium permanganate in alkaline medium there was isolated terephthalic acid, which then was converted to dimethyl terephthalate with m. p. 140° (from alcohol). According to data [13]: m. p. 140°.

Oxidation of p-sec-butyltoluene was run in the presence of 5 mg/mole of manganese resinate at 110° using as oxidation initiator the isopropylbenzene hydroperoxide, as above.

The rate of formation of the hydroperoxide was not over 0.5% per hour* during the first 4 hrs of the process, with a gradual decrease of it in the latter stages of the oxidation. After 16 hrs of oxidation there was accumulated but 4% of the hydroperoxide in the hydrocarbon. The mean rate of oxygen absorption during this process was 0.12-0.14 liter/hr per mole of hydrocarbon during the first 4 hrs of reaction and decreased slightly in the subsequent period of the process. Thus, the major part of the hydroperoxide decomposed during the very process of oxidation. The oxidation of the recovered p-butyltoluene (purified by treatment with sulfuric acid and distillation) was found to proceed at the same rate.

p-sec-Butylbenzaldehyde was isolated from the oxidized hydrocarbon by the technique analogous to that used for the extraction of cumyl aldehyde from oxidized p-cymene, in the form of 2,4-dinitrophenylhydrazone. M. p. 175-177.5° (from alcohol).

Found %: N 16.99. $C_{17}H_{18}O_4N_4$. Calculated %: N 16.35.

p-Methylacetophenone was isolated from the oxidized p-sec-butyltoluene by the method described for the isolation of this substance from oxidized p-cymene, in the form of 2,4-dinitrophenylhydrazone. M. p. 251-252°. A mixed melting point showed no depression.

Isolation of hydroperoxide. Oxidized p-sec-butyltoluene (184 g) containing 3.95% of hydroperoxide was freed of acid admixtures by washing with 5% sodium hydroxide and was then dried. After distillation of the unoxidized butyltoluene in vacuo (54-57° at 5 mm) there remained in the flask a product containing 72.18% of monohydroperoxide. By a series of successive distillations of this substance in vacuo of 0.03 mm in a flask with a low-set side arm, there was obtained 0.8 g of a fraction boiling at 73-75° ($n^{20}D$ 1.5200) showing in iodometric analysis the content of 81.85% of hydroperoxide. A sample (0.7643 g) of the hydroperoxide was dissolved in 5 ml of ether and was decomposed by a mixture of sulfuric acid (d 1.84) and ether. The decomposed mass was neutralized with potassium carbonate and was analyzed for the p-cresol content (see above) and for methyl ethyl ketone content (by the method of acetone determination in decomposition of p-cymene hydroperoxide). The yield (in % of theoretical): p-cresol 100, methyl ethyl ketone 78.7. Methyl ethyl ketone was identified in the form of 2,4-dinitrophenylhydrazone. M. p. 115° (from alcohol). Mixed melting point gave no depression.

Owing to the insignificant amount of p-cresol, we identified it only by a qualitative test [14].

## SUMMARY

1. The oxidation of p-cymene and p-sec-butyltoluene by atmospheric oxygen in liquid phase at 110° in the presence of manganese resinate was examined. For p-cymene there was also run an oxidation in aqueous alkaline emulsion at 95°.

2. It was found that in oxidation of p-cymene and p-sec-butyltoluene oxygen reacts with both the primary and the tertiary $\alpha$-carbon atoms. In case of p-cymene it was established that the direction of the reaction is not changed by alteration of the oxidation method.

3. Hydroperoxide of p-cymene and hydroperoxide of p-sec-butyltoluene were prepared. The isolated hydroperoxides have the structure of tertiary hydroperoxides.

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# LIQUID PHASE OXIDATION OF ALKAROMATIC HYDROCARBONS BY ATMOSPHERIC OXYGEN

## OXIDATION OF p-DI-SEC-BUTYLBENZENE

### V. V. Fedorova and P. G. Sergeev

Liquid phase oxidation of dialkyl substituted benzenes in which both substituents are alike had not been studied much up to this time. The exceptions are only p-xylene [1] and m- and p-diisopropylbenzenes [2], from which only monohydroperoxides have been prepared, while the diisopropylbenzenes also yielded the dihydroperoxides. However, even in these cases the kinetics and mechanism of the formation of dihydroperoxides have not been studied. At the same time, the possibility of formation of p- and m-dihydroperoxides by oxidation of such hydrocarbons has not only the scientific but also the practical points of interest as a possible new path for the preparation of hydroquinone and resorcinol.

We conducted a study of the oxidizability of p-di-sec-butylbenzene with atmospheric oxygen in liquid phase at 110° in the presence of minimum amounts of a catalyst which was soluble in the hydrocarbon. The rate of oxidation was 0.22-0.25% of active oxygen per hour. It was found that in the oxidation of this hydrocarbon there are formed both the mono- and the dihydroperoxides. The monohydroperoxide, which was isolated by us in the free state, decomposed under the action of sulfuric acid with formation of p-sec-butylphenol and methyl ethyl ketone by the scheme:

$$\underset{\underset{C_2H_5}{|}}{\overset{\overset{CH_3}{|}}{HC}}-\!\!\left\langle\bigcirc\right\rangle\!\!-\underset{\underset{C_2H_5}{|}}{\overset{\overset{CH_3}{|}}{C}}-OOH \xrightarrow{H_2SO_4} \underset{\underset{C_2H_5}{|}}{\overset{\overset{CH_3}{|}}{HC}}-\!\!\left\langle\bigcirc\right\rangle\!\!-OH + CH_3COC_2H_5$$
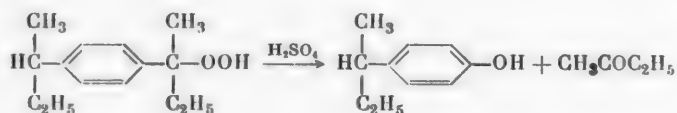
The dihydroperoxide, obtained in a mixture with monohydroperoxide, was transformed in the presence of sulfuric acid into hydroquinone and methyl ethyl ketone. For clarification of the practical possibility of preparation of hydroquinone by oxidation of p-di-sec-butylbenzene, we determined the rate of accumulation of the dihydroperoxide in the course of the oxidation.

These determinations were based on the fact that in the reaction of sulfuric acid with peroxide compounds contained in the oxidized p-dibutylbenzene, there are obtained p-butylphenol, hydroquinone and methyl ethyl ketone. By determining the content of these products in the decomposed mass, it was easy to calculate what amounts of mono- and dihydroperoxides were present in the oxidized p-dibutylbenzene prior to the decomposition. Here we neglected, of course, the presence of other products of decomposition of the hydroperoxides, owing to the insignificant amounts of them.

On the basis of data obtained in this manner we constructed the curves of the rates of formation of mono- and dihydroperoxides after a 15-hr oxidation of p-di-sec-butylbenzene.

The form of these curves (see Figure) shows that the rate of formation of the dihydroperoxide is considerably smaller than that of the monohydroperoxide and that, evidently, the dihydroperoxide is formed by oxidation of the monohydroperoxide.

Preparation of p-di-sec-butylbenzene. This hydrocarbon was prepared by us by alkylation of benzene with 2-butene in the presence of aluminum chloride (5% of the weight of benzene) at 50-70°. The product isolated by fractionation was purified by being shaken with sulfuric acid (d 1.84) and was washed with alkali and water; after being dried it was distilled.

B. p. 91.5-92° at 3 mm, $n^{20}D$ 1.4878, $d_4^{20}$ 0.8572. According to data [3]: b. p. 240° at 760 mm, $n^{20}D$ 1.4878, $d_4^{20}$ 0.8573.
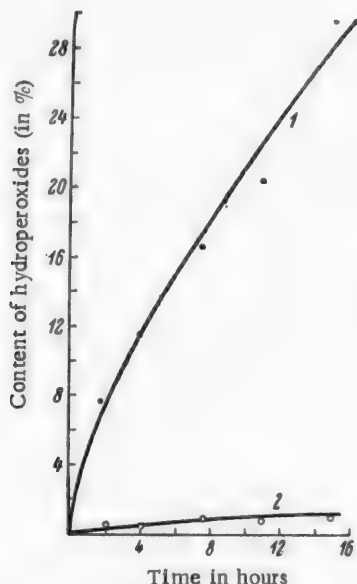


Accumulation of mono- and dihydroperoxides in oxidation of p-di-sec-butylbenzene: 1) mono-hydroperoxide; 2) dihydroperoxide.

The structure of the isolated product as that of p-di-sec-butylbenzene was confirmed by its oxidation with potassium permanganate in alkaline medium to terephthalic acid, from which there was then prepared the dimethyl ester with m. p. 140° (from alcohol). According to data [4]: m. p. 140°.

Oxidation was run in a cylindrical glass vessel with a widened portion near the top, provided with a reflux condenser connected to a trap, thermometer, stirrer and a capillary for air inlet. The hydrocarbon with the catalyst dissolved in it (5-7 mg/mole of manganese resinate) and with a few drops of oxidation initiator (hydroperoxide of p-di-sec-butylbenzene containing 5.85% of active oxygen) was heated to 110°, after which air was introduced into it at the rate of 8-10 liters/hr per mole. The mean rate of formation of hydroperoxide was 3-3.5% per hour,[*] and remained at this level for 12-14 hrs, i. e., the decomposition of the hydroperoxides during the oxidation was quite insignificant and the hydroperoxides themselves were completely stable during the accumulation process. After 14 hrs of oxidation there was accumulated up to 48.5% of hydroperoxide.[*] The rate of oxygen absorption was 0.6-0.8 liters/hr per mole and also remained constant during the oxidation.

Oxidation of the recovered p-di-sec-butylbenzene obtained by distillation in vacuo from the oxidation products and purified with sulfuric acid proceeded at the same rate as above.

Isolation of dihydroperoxide of p-di-sec-butylbenzene. Oxidized p-di-sec-butylbenzene (103 g) containing 3.53% of active oxygen was washed with 5% soda solution for the removal of acidic products and was distilled in vacuo (2.5 mm) after drying. After the separation of the unoxidized hydrocarbon at 90° there remained in the pot 45.58 g of a liquid containing 6.64% of active oxygen. This residue was diluted with 20 ml of ether and, with cooling, there was added to it 17.5 ml of 40% sodium hydroxide, the addition being made gradually. The resulting precipitate of sodium salts of hydroperoxides was washed with ether by decantation, pressed dry with a spatula in a beaker and was covered with water. Carbon dioxide was passed through the resulting suspension. The hydroperoxides liberated thereby were then extracted with ether, after the distillation of which there remained a viscous liquid containing 9.54% of active oxygen; $n^{20}D$ 1.5243.

Found %: C 68.20, 67.47; H 8.84, 8.71; active O 9.54. $C_{14}H_{22}O_2$. Calculated %: C 75.63; H 9.91; active O 7.20. $C_{14}H_{22}O_4$. Calculated %: C 66.14; H 8.66; active O 12.59.

The presence of the dihydroperoxide in the product was confirmed by the reaction with sulfuric acid.

A small amount of the product (about 2 g) was dissolved in ether and to it was added dropwise a solution of several drops of sulfuric acid (d 1.84) in ether. The temperature of the reaction mixture was kept under 45°. To the decomposed mixture there was added 75 ml of 30% aqueous solution of ferric chloride and the mixture

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[*] Calculated provisionally on monohydroperoxide.

was shaken energetically. Hydroquinone is thereby readily oxidized to benzoquinone [5] which was then extracted with chloroform. For reconversion of benzoquinone back to hydroquinone there was added to the separate chloroform layer 50 ml of 10% sulfuric acid and 65 ml of 10% potassium iodide. The mixture containing the separated iodine was treated with sodium thiosulfate solution. The hydroquinone which is insoluble in chloroform distributed itself in the aqueous layer from which it was then extracted with ether. After the distillation of ether there remained crystals of hydroquinone. The yield was about 0.3 g. M. p. 168-169°. Mixed melting point gave no depression.

Found %: C 65.64, 65.97; H 5.70, 6.17. $C_6H_6O_2$. Calculated %: C 65.44; H 5.49.

Isolation of monohydroperoxide of p-di-sec-butylbenzene. As a result of several experiments on oxidation of p-di-sec-butylbenzene and separation of the dihydroperoxide from the resulting reaction mixture as described above, there was collected a product (total amount of 107.55 g; active oxygen content 5.43%), which was fractionated at the pressure of 0.005 mm. The results of distillation and the analyses of the fractions are given in the Table.

| Fraction no. | Boiling point | Wt. of fractions in g | Content (in %) | |
| --- | --- | --- | --- | --- |
| | | | of active oxygen | of monohydro-peroxide |
| 1 | 27—30° | 6.48 | 2.35 | 32.29 |
| 2 | 37—60.5 | 28.70 | 2.37 | 32.53 |
| 3 | 61—65 | 14.49 | 6.49 | 89.30 |
| 4 | 66—78 | 26.67 | 7.10 | 97.65 |
| Residue | Above 78 | 21.97 | 6.2 | |
| Losses | | 9.24 | | |

The 4th fraction was p-di-sec-butylbenzene monohydroperoxide: $d^{20}$ 0.986, $n^{20}$D 1.5110, $MR_D$ 67.53; calculated 67.29.

Found %: C 76.21; H 10.25; active O 7.10. $C_{14}H_{22}O_2$. Calculated %: C 75.63; H 9.97; active O 7.20.

It is a rather viscous liquid with a penetrating odor characteristic of peroxides; it does not decompose noticeably on being heated to 110°.

A sample of the monohydroperoxide (9.12 g) was dissolved in ether and decomposed by careful addition of a mixture of sulfuric acid and ether at 45°. The decomposed mixture was neutralized with potassium carbonate and analyzed. For binding the p-butylphenol there was added to the reaction mixture some 10% sodium hydroxide solution, after which the methyl ethyl ketone was separated by steam distillation and was analytically determined in the distillate by its reaction with hydroxylamine hydrochloride. For identification of methyl ethyl ketone its 2,4-dinitrophenylhydrazone was isolated. M. p. 112-113°. Mixed melting point gave no depression.

In the alkaline solution, remaining after the distillation of methyl ethyl ketone, in a separate sample there was iodometrically determined the content of p-sec-butylphenol; from the main body of the solution there was isolated p-sec-butylphenol by acidification; this formed colorless crystals with characteristic odor of freshly tanned leather; m. p. 53°. According to data [6]: m. p. 53-54°.

Found %: C 78.75; H 10.10. $C_{10}H_{14}O$. Calculated %: C 79.90; H 9.39.

In the analysis of the decomposed mass there was found (in % of theoretical): p-sec-butylphenol 99.2 and methyl ethyl ketone 71.2.

Determination of rates of formation of mono- and dihydroperoxides. p-Di-sec-butylbenzene (150 ml) was oxidized under the conditions used by us above. Samples were taken periodically in which the content of active oxygen was determined after which the decomposition of the hydroperoxides with sulfuric acid was performed. The decomposed sample of the reaction mixture was divided into two parts: from one part there were steam distilled, in the presence of sodium bicarbonate solution, the methyl ethyl ketone and the p-sec-butylphenol (hydroquinone remains in the pot under these conditions) and their mixture was separated and analyzed by the method described above as used for the analysis of the products of acidic decomposition of monohydroperoxides.

In the second portion we determined the content of hydroquinone by the method developed for its determination in the presence of resorcinol and other phenols [5].

On the basis of the values of content of p-sec-butylphenol and hydroquinone in the decomposed mixture, as obtained above, we calculated the amounts of mono- and dihydroperoxides present in the oxidized hydrocarbon prior to the decomposition and from these data we constructed the curve of the change of content of hydroperoxides with time.

## SUMMARY

1. There was examined the oxidizability of p-di-sec-butylbenzene with atmospheric oxygen in liquid phase at 110° in the presence of a catalyst (manganese resinate, 5-7 mg/mole).

2. It was shown that in this oxidation there are formed mono- and dihydroperoxides; the monohydroperoxide was isolated in the free state.

3. The principal technique for the separate determination of mono- and dihydroperoxides in the reaction mixture was developed and on this basis there was studied the rate of formation of mono- and dihydroperoxides in oxidation of p-di-sec-butylbenzene.

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# A NEW METHOD FOR THE PREPARATION OF QUINALDINE BASES AND N-ARYLQUINALDINIUM SALTS BY THE CONDENSATION OF ARYLAMINES WITH ALDEHYDES. XX.

## V. I. Minkin and B. I. Ardashev

Recent investigations permit the conclusion that the quinaldine synthesis by the method of Doebner and Miller [1] proceeds in two stages: the formation of diethylideneaniline bases (Eibner-Eckstein bases) and their cyclization to quinaldine derivatives [2-9].

The optimum conditions for the formation of the diethylideneaniline bases [7] and for the preparation of the quinaldines from them [8] differ considerably; we therefore made an attempt to separate these stages of the synthesis by condensing acyl anilides with aldehydes in the presence of sodium alcoholate and subsequently cyclizing the products in acid medium. The reaction mechanism basically seems to us to proceed according to the following scheme:
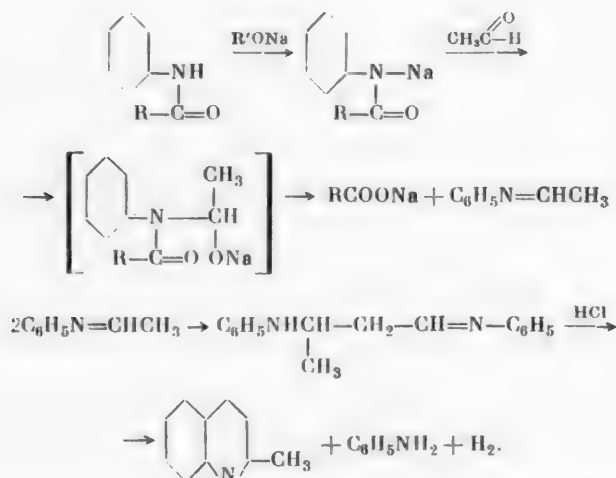


Some quinaldine bases, for example, 6-methoxy-, 6-ethoxy-, and 5,6-benzoquinaldine and others, were obtained in yields amounting to 98% of theoretical calculated on the Eibner-Eckstein base, which was considerably higher than the yields from the methods previously described.

A similar method of carrying out the reaction with separate condensation and cyclization processes can be employed also for the synthesis of the recently described N-arylquinaldinium salts [10-13].

According to the proposed method, a diarylamine is condensed with acetal in nitrobenzene solution, whereupon cyclization is easily obtained just by steam-distilling off the solvent from an acid medium. Thanks to the elimination of the side reaction forming diarylmethane derivatives, which occurs in acid medium [14], and to the presence of an oxidizer, the yield of some of the N-arylquinaldinium derivatives amounts to 40% of the theoretical calculated on the amine taken.

Of the two possible schemes for the main course of the reaction [9]

$$ArNHAr + CH_3C{\overset{O}{\underset{H}{\big<}}} \longrightarrow \underset{Ar}{\overset{Ar}{\big>}}NCHOHCH_3 \xrightarrow[-H_2O]{CH_3C{\overset{O}{\big<}}_H} \underset{Ar}{\overset{Ar}{\big>}}N\underset{CH_3}{\underset{|}{C}}HCH_2C{\overset{O}{\underset{H}{\big<}}} \quad \text{and perhaps} \quad (I)$$

$$\underset{Ar}{\overset{Ar}{\big>}}NCH=CH_2 \quad (II)$$

$$2\,\underset{Ar}{\overset{Ar}{\big>}}NCH=CH_2 \longrightarrow \underset{Ar}{\overset{Ar}{\big>}}N\underset{CH_3}{\underset{|}{C}}HCH=CHN{\overset{Ar}{\big<}}_{Ar} \xrightarrow{HCl} \text{(quinaldinium salt)} + ArNHAr + H_2$$
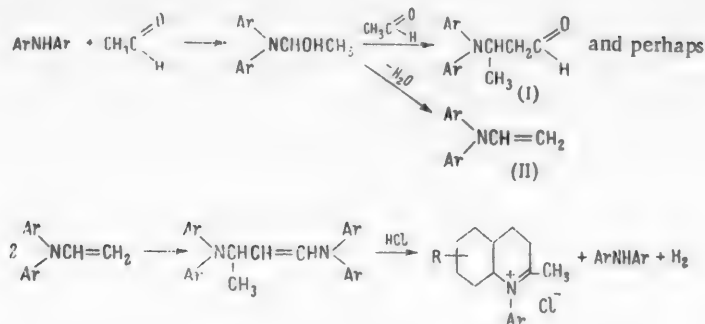
the first must be excluded, since the Beyer reaction [15] does not go under such conditions.

The production of the dimer of vinyldiphenylamine also is confirmed by the formation of quinaldine from ethylaniline by condensation with acetylene in neutral medium [16] and by the considerable increase in yields of N-arylquinaldinium salts on replacement of acetaldehyde by vinyl ether [17].

EXPERIMENTAL

## I. Synthesis of Quinaldine Bases

Formanilide and acetanilide were used for the reaction and gave similar results. Use of the free amine lowered the yield of the quinaldine product approximately by half. As a solvent we used anhydrous ethyl, iso-butyl, and isoamyl alcohol, obtaining the best results by the use of isobutyl alcohol.

1. Preparation of 6-methylquinaldine. 3 g of sodium was dissolved in 100 ml of isobutyl alcohol, and 13.5 g of formo-p-toluidide was added with mechanical stirring. The insoluble sodium derivative formed immediately, after which 15 ml of paraldehyde was run in. Moderate boiling of the mixture was continued for 3.5 hrs with constant vigorous stirring. On cooling of the reaction mixture, 40 ml of water, 40 ml of concentrated hydrochloric acid, and 1.5 g of zinc chloride were added and the mixture was kept boiling gently for another 3.5 hrs. The alcohol was steam-distilled off, the residue in the flask was made alkaline, and the base was also steam-distilled. 6-Methylquinaldine was isolated as a complex with potassium ferrocyanide [18] that was decomposed with 10% sodium hydroxide. Yield 7.5 g (48% calculated from the formo-p-toluidide taken, or 96% calculated from the Eibner-Eckstein base). B. p. 118-124° at 2-3 mm, m. p. 58-59°. Picrate, m. p. 187°; methiodide, m. p. 242°.

Found %: N 8.75. $C_{11}H_{11}N$. Calculated %: N 8.92.

2. 6,8-Dimethylquinaldine. 3 g of sodium, 100 ml of isobutyl (or ethyl) alcohol, and 12.1 g of formo-m-xylidide were used. No precipitate of sodium derivative formed. On solution of the formo-m-xylidide, 15 ml of paraldehyde was added, whereupon the solution changed color and a precipitate gradually separated, which was identified qualitatively as sodium formate. The mixture was boiled for 3 hrs, 40-50 ml of solvent was distilled off, 50 ml of water, 50 ml of concentrated hydrochloric acid, and 1.3 g of zinc chloride were added, and boiling was continued for another 3 hrs. 6,8-Dimethylquinaldine was isolated as in Expt. 1. Yield 6.8 g (49%). B. p. 255-270°. Picrate, m. p. 185°.

Found %: N 8.26. $C_{12}H_{13}N$. Calculated %: N 8.19.

3. Quinaldine. 2.8 g of sodium, 100 ml of isoamyl alcohol, 12.1 g of formanilide, and 14 ml of paraldehyde were used. The experiment was similar to Expt. 1. Yield of quinaldine 2.2 g (15%). B. p. 237-250°. Picrate, m. p. 191-192°.

Found %: N 9.90. $C_{10}H_9N$. Calculated %: N 9.79.

4. 6-Methoxyquinaldine. 3 g of sodium, 100 ml of isobutyl alcohol, 15.1 g of formo-p-anisidide, and 17 ml of paraldehyde were used. After 3.5 hrs boiling, 45 ml of concentrated hydrochloric acid was added and

boiling was continued for 1 hr. Yield 6.1 g (35%). B. p. 280-292°, m. p. 64°. Picrate, m. p. 217°; methiodide, m. p. 236-238°; quinophthalone, m. p. 155°.

Found %: N 8.21. $C_{11}H_{11}ON$. Calculated %: N 8.09.

5. 8-Methoxyquinaldine. 3 g of sodium, 100 ml of isobutyl alcohol, and 16.5 g of aceto-o-anisidide were used. Upon addition of 17 ml of paraldehyde the mixture darkened and a precipitate gradually separated, in which sodium acetate was detected. After 4.5 hrs boiling, 40 ml of water, 40 ml of concentrated hydrochloric acid, and 1.5 g of zinc chloride were added, and boiling was continued for another 3.5 hrs. Then the mixture was diluted with 150-200 ml of water and heated with activated carbon, and on cooling 8-methoxyquinaldine was precipitated from the filtrate with potassium ferrocyanide. Yield 4.7 g (28%). B. p. 121-122°. Mercury salt, m. p. 243°.

Found %: N 8.30. $C_{11}H_{11}ON$. Calculated %: N 8.09.

6. 6-Ethoxyquinaldine was prepared from 16.1 g of formo-p-phenetidine, 15 ml of paraldehyde, and 3 g of sodium in 100 ml of isobutyl alcohol after boiling for 4 hrs and then in acid medium for 3 hrs. The isolation was carried out as in Expt. 5. Yield 8.9 g (48%). B. p. 169-175° at 14 mm, m. p. 68°. Picrate, m. p. 193°; methiodide, m. p. 157°.

Found %: N 7.25. $C_{12}H_{13}ON$. Calculated %: N 7.48.

7. 5,6-Benzoquinaldine. 3 g of sodium, 100 ml of isobutyl alcohol, 18.5 g of aceto-β-naphthalide, and 15 ml of paraldehyde were boiled for 7 hrs, and after addition of 40 ml of water, 40 ml of concentrated hydrochloric acid, and 0.5 g of zinc chloride, for 3.5 hrs more. The mixture was diluted to 200 ml and treated with activated carbon. When the filtrate cooled, flakes of the difficultly soluble hydrochloride of 5,6-benzoquinaldine precipitated. Yield of the salt 10.3 g (45%); 5,6-benzoquinaldine was isolated from it by alkalizing. M. p. 79-80°. Picrate, m. p. 228° [19].

Found %: Cl 15.28. $C_{14}H_{12}NCl$. Calculated %: Cl 15.43.

8. 3-Ethyl-6-methylquinaldine. 3 g of sodium, 100 ml of isobutyl alcohol, 13.5 g of formo-p-toluidide, and 24 ml of propionaldehyde were used. The experiment was similar to Expt. 5. Yield 1.8 g (10%). B. p. 284-293°, m. p. 51°. Picrate, m. p. 178°.

Found %: N 7.40. $C_{13}H_{15}N$. Calculated %: N 7.53.

9. N-Phenylquinaldine perchlorate. 16.9 g of diphenylamine was added to a solution of 3 g of sodium in 100 ml of isobutyl alcohol, 15 ml of paraldehyde was added, and the mixture was boiled for 5 hrs. After acidification with 25 ml of concentrated hydrochloric acid, addition of 12 g of o-nitrophenol, and boiling for another 3 hrs, N-phenylquinaldine perchlorate was isolated as in Expt. 10. Yield 3.5 g (11%). B. p. 155-158°.

## II. Synthesis of N-Arylquinaldinium Salts

10. N-Phenylquinaldine perchlorate. 16.9 g of diphenylamine, 30 ml of acetal (use of paraldehyde gives almost the same results), and 100 ml of nitrobenzene were boiled gently for 5-6 hrs. 80 ml of concentrated hydrochloric acid was added and the nitrobenzene was slowly steam-distilled off. The unreacted diphenylamine was completely resinified by this treatment and remained on the walls of the flask. The nearly clear solution was poured off, treated with activated carbon, and evaporated to a volume of 50-75 ml, from which N-phenylquinaldine perchlorate was precipitated by the dropwise addition of concentrated perchloric acid. Yield 7 g (22%). M. p. 158-160°. After recrystallization from water m. p. 162-163° (according to [10], m. p. 158-159°; according to [12], 160-162°).

Found %: Cl 11.21. $C_{16}H_{14}O_4NCl$. Calculated %: Cl 11.09.

When the reaction was carried out in nitrobenzene solution and diphenylamine hydrochloride was used instead of the free amine, the yield was lowered to 12-14%.

11. N-p-Tolyl-6-methylquinaldine perchlorate. 9.5 g of di-p-tolylamine, 18 ml of acetal, and 50 ml of nitrobenzene were heated for 5 hrs. 50 ml of concentrated hydrochloric acid was added and the nitrobenzene was steam-distilled off. The further treatment was similar to Expt. 10. Yield 6.7 g (40%). M. p. 188-189°. After recrystallization from aqueous ethanol m. p. 192-193°.

Found %: Cl 10.02. $C_{18}H_{18}O_4NCl$. Calculated %: Cl 9.91.

12. N-Phenylmethylquinaldine perchlorate. 6.9 g of phenyl-p-tolylamine, 15 ml of acetal, and 45 ml of nitrobenzene were used. 3.5 g (28%) of N-phenyl-6-methylquinaldine perchlorate was obtained. M. p. 154-155°.

Found %: Cl 10.77. $C_{17}H_{16}O_4NCl$. Calculated %: Cl 10.63.

13. N-Phenyl-5,6-benzoquinaldine perchlorate. 9 g of phenyl-β-naphthylamine, 13 ml of acetal, and 45 ml of nitrobenzene were used. 6.1 g (40%) of N-phenyl-5,6-benzoquinaldine perchlorate was obtained. M. p. 154-156°. After recrystallization from water, m. p. 160°.

Found %: Cl 9.71. $C_{20}H_{16}O_4NCl$. Calculated %: Cl 9.60.

## SUMMARY

1. A new method has been developed for the preparation of quinaldine bases and N-arylquinaldinium salts by the condensation of acylated arylamines and diarylamines with aldehydes.

2. A mechanism has been proposed for these syntheses.

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# REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

## XI. CAUSES OF THE COLORATION OF SOME DIAZONIUM AND HETEROCYCLIC

## AMMONIUM SALTS

### D. Z. Zavel'skii and L. A. Lishnevskaia

In previous articles [1-3] we have described the synthesis and properties of diazonium arylsulfamates and acylamidoarylsulfonates and have made some suggestions concerning the causes of the coloration of these salts.
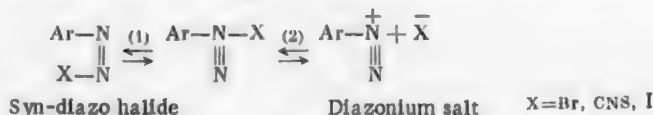
The problem in the present paper is the examination of the colored diazonium salts known in the literature and of compounds related to them and comparison of them with salts synthesized by us for the purpose of ascertaining the reasons for the appearance of color in organic salts of which the cations and anions are colorless.

It is known that diazonium sulfates, nitrates, chlorides, and other diazonium salts in which the anions are colorless are themselves also colorless. However, Hantzsch [4] noted that the bromides, thiocyanates, and iodides of diazo compounds are colored. For example, phenyl-, anisyl-, and pseudocumyldiazonium bromides were almost colorless or light yellow, but mono- and polyhalogenated phenyldiazonium compounds were colored from yellow to red. In this instance, the greater the number of halogen substituents, the deeper was the color and the more explosive the diazo salt. Somewhat more intensely colored and explosive diazo thiocyanates were synthesized by Hirsch [5]. The diazo iodides were especially deeply colored and explosive. The iodides of the strong 2,4,5- and 2,4,6-trimethyl- and 4-methoxyphenyldiazonium bases were colored golden yellow and were so unstable that it was difficult to isolate them in pure form. 2,4-Dibromo-, 2,6-dibromo-, and 2,6-diiodophenyldiazonium iodides were colored, respectively, dark orange, intense red, and blood red and decomposed even in the isolated process.

Thus, in diazonium bromides, thiocyanates, and iodides the depth of color grows with an increase in the electrophilic nature of the substituents in the aryl ring of the diazonium component. A perfectly similar rule is observed for the diazonium acylamidoarylsulfonates and arylsulfamates studied by us, although the extent of deepening of the color in the latter is much greater. The series of salts enumerated have the general property of being colored only in the solid state and yielding colorless or light yellow solutions.

The diazo thiocyanates and iodides are less soluble than the corresponding chlorides. In exactly the same way, the diazonium arylsulfamates and acylamidoarylsulfonates are much less soluble than the corresponding chlorides. It may also be noted that the solubility of the arylsulfamates, as a rule, decreases with an increase in the electrophilic nature of the substituents in the benzene ring of the diazonium component. For example, the 4-chlorophenyldiazonium salt of phenylsulfamic acid dissolves in water to the extent of 7.5%, and the 4-nitrophenyldiazonium salt to the extent of only 3.5%.

To explain the reasons for the coloration and the explosiveness of the diazo bromides, thiocyanates, and iodides in the solid state and their colorlessness in aqueous solution, Hantzsch advanced the suggestion that for these salts as for the diazo cyanides [6] an equilibrium exists between the syn-diazo halide, the diazonium halide, and its ions

$$
\begin{array}{ccc}
\text{Ar—N} & \xrightarrow{(1)} \text{Ar—N—X} & \xrightarrow{(2)} \text{Ar—}\overset{+}{\text{N}} + \overset{-}{\text{X}} \\
\overset{\parallel}{\text{X—N}} & \overset{\parallel}{\text{N}} & \overset{\parallel\parallel}{\text{N}} \\
\text{Syn-diazo halide} & \text{Diazonium salt} & \text{X=Br, CNS, I}
\end{array}
$$

In Hantzsch's opinion, the diazonium salts should be colorless and stable, like ammonium salts with "pentavalent" nitrogen, and the syn-diazo halides should be colored like azo compounds and unstable, even explosive, like the halogen compounds of nitrogen ($NCl_3$, $NBr_3$, $NI_3$). The author thought that the equilibrium (1) between the syn-diazo and the diazonium forms exists in the solid salts, which are solid solutions of the one form in the other, and equilibrium (2) exists in aqueous solutions. In case the diazo group is linked with chlorine, both equilibria are moved to the right (the diazo chlorides are colorless). When chlorine is replaced by bromine, iodine, or a thiocyanate group, the equilibria shift to the left, in the direction of the azo form.

Euler and Hantzsch [7] have shown that movement of the equilibrium to the left is favored not only by the negativity of the substituents and increase in the atomic weight of the halogen, but also by replacement of the water by alcohol (a less dissociated solvent), elevation of the temperature, and decrease in the acidity of the medium. However, Hantzsch did not explain why the presence on the ring in the diazo halides of electronegative substituents (and heavy halogens or thiocyanate as anions) results in a deepening of their color.

Saunders [8], considering the work of Hantzsch, came to the conclusion that ". . . as the basicity of the diazonium diminishes and the acidity of the acid ion decreases, the color of the salts deepens." However, this generalization is in error, since of the three acids whose diazonium salts are colored only thiocyanic acid is comparatively weak ($K = 0.14$). With regard to hydrobromic and hydriodic acids, they are stronger, not weaker, than hydrochloric acid (0.1 N HCl solution is 92.6% dissociated, HBr 93.5%, and HI 9.50%). However, the depth of coloration of the diazo thiocyanates is between that of the bromides and the iodides. From this it follows that, first, the decrease in the acidity of the anion is not the cause of the coloration of the diazo halides of Hantzsch, and, second, if the diazonium structure is generally admitted for the diazo chlorides, then the diazo bromides and diazo iodides as salts of still stronger acids must be considered diazonium salts also, and not syn-diazo halides.

Hantzsch's views on the causes for the coloration of the diazo halides are an essential part of his theory of the structure of the diazo compounds and are usually cited in monographs on the diazo compounds [8, 9]. However, it will be further shown that the coloration of the diazo halides is not caused by a transition to the azo form, but by other factors.

A detailed examination of the literature on the question under consideration has confirmed that all the halides of ammonia and of its alkyl- and simple aryl-substituted derivatives are colorless. An interesting exception is the salts of the nitrogen-containing heterocycles with positively charged tetravalent nitrogen.

In Meyer-Jacobson's handbook [10] it is pointed out that methylquinolinium and methylisoquinolinium iodides are colored bright yellow, while the corresponding cations and anions are colorless. Decker [11] found that methylacridinium chloride is colored yellow, like the cation of this salt, and the iodide is orange-red. Claus [12], Decker [13], and Kaufmann [14], who introduced halogens and nitro groups into the quinolinium nucleus, synthesized the corresponding iodides, which were colored from red to almost black. Kröhnke [15] synthesized a number of iodides, bromides, thiocyanates, and other salts of different pyridinium, quinolinium, and isoquinolinium derivatives, in which the key nitrogen atom was substituted not with methyl, but with a benzyl, phenacyl, or aryl group, whereupon he introduced electrophilic and electron-donor substituents into the ring of the heterocycle, or of the benzyl, phenacyl, or aryl group.

Kröhnke studied in detail the effect of the different substituents and their position on the depth of color of the salts, which he called cycloammonium salts, since they contain an onium nitrogen in the aromatic ring. The author came to the conclusion that the more electrophilic the substituted cycloammonium cation and the more complex the aromatic ring containing the salt-forming nitrogen, the deeper was the color of the salts formed by them. The color of the salts deepened on passing from the bromides to the thiocyanates and from the thiocyanates to the iodides. Upon the solution in water, colored cycloammonium salts were decolorized as a result of dissociation into colorless ions. In solvents with a lower dielectric constant than water the cycloammonium salts decolorized less, or not at all. Heating of the solutions of the colored salts in solvents with a small dielectric constant led to a deepening of the color, and cooling to a weakening of it. Fusion or even simple heating of the solid cycloammonium salts also deepened their color.

Consequently, all the properties of the colored cycloammonium salts are highly similar to the properties of the diazo halides studied by Hantzsch and to those of the arylsulfamates and acylamidoarylsulfonates described by us. At the same time, from an examination of the formula for the diazonium cation and the cycloammonium cation it is apparent that if the former is capable of transition to a diazo cation with trivalent nitrogen (for example,

in the formation of azo dyes), then a similar transition for the latter with the formation of a carbonium cation is only slightly probable.
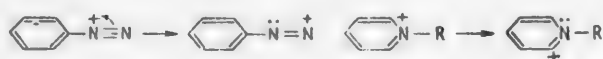


Hence, contrary to Hantzsch's opinion, the color of the diazonium halides and salts of the arylsulfamic and acylamidoarylsulfonic acids must not be related at all to the transition of the diazonium cation to the diazo cation, since in the cycloammonium salts the deepening of color with an increase in the electrophilic nature of the cycloammonium cation and with a rise in the atomic weight of the halide anion occurs in the presence of an indisputable tetravalent salt-forming nitrogen.

Therefore, the cause of the coloration in the compounds examined must be sought in the special nature of the salt bond between the onium nitrogen and the anions of the heavy halides or of some other compounds. For this purpose, it is useful to examine first the behavior of the halide anions in inorganic salts.

As is well known, under the influence of an electric field the electron shell of an ion, especially the outer shell, is deformed more the farther it is from the attracting nucleus. Consequently, the deformation of the iodide or bromide anion under the influence of one and the same cation is considerably greater than that of the chloride or fluoride anion. However, Fajans [16] has already shown that the greater the deformation of the electron shells of the anion and cation, the more the character of the bond between these ions diverges from heteropolar toward homeopolar.

The mutual intrusion of the electron shells of the cation and anion in some salts causes the appearance of color in them. In the table presented below we have collected some data on colored inorganic halides.

From this table it is apparent that the iodides are always more strongly colored than the bromides. Of the ions with one charge, only $Ag^+$ with an incomplete N electron layer is capable of forming colored salts with the heavy halogens. Of the doubly charged ions, 4 are capable of forming colored salts, and $Cu^{2+}$ with an incomplete M layer forms the darkest and most unstable salts. Among the ions with a triple charge, thallium, which is electronically similar to doubly charged $Hg^{2+}$, yields halides that are much more deeply colored than the mercury salts. $Ti^{4+}$ and $Zr^{4+}$ with 4 charges, in spite of their small atomic numbers, yield colored iodides. In each of the latter cations the outer electron shell is unfilled.

Summary of Some Data on the Colored Inorganic Halides

| Element | Atomic no. | Ion | Completeness of electron layers | | | | | | Ionic radius | Formulas and colors of salts* | |
| | | | K | L | M | N | O | P | | iodides | bromides |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Ag | 47 | $Ag^+$ | 2 | 8 | 18 | 18 | | | 1.13 | AgI yellow | AgBr light yellow |
| Cu | 29 | $Cu^{2+}$ | 2 | 8 | 17 | | | | 0.82 | $CuI_2$ does not exist | $CuBr_2$ brown-black** |
| Ge | 32 | $Ge^{2+}$ | 2 | 8 | 18 | 2 | 2 | | 0.98 | $GeI_2$ orange | $GeBr_2$ yellow |
| Sn | 50 | $Sn^{2+}$ | 2 | 8 | 18 | 18 | 18 | | 1.02 | $SnI_2$ red | $SnBr_2$ yellow |
| Hg | 80 | $Hg^{2+}$ | 2 | 8 | 18 | 32 | 18 | | 1.12 | $HgI_2$ red | $HgBr_2$ colorless |
| Pb | 82 | $Pb^{2+}$ | 2 | 8 | 18 | 32 | | 2 | 1.32 | $PbI_2$ yellow | $PbBr_2$ colorless |
| In | 49 | $In^{3+}$ | 2 | 8 | 18 | 18 | | | | $InI_3$ yellow | $InBr_3$ colorless |
| Tl | 81 | $Tl^{3+}$ | 2 | 8 | 18 | 32 | 18 | | 1.05 | $TlI_3$ black | $TlBr_3$ yellow |
| Ti | 22 | $Ti^{4+}$ | 2 | 8 | 8 | | | | 0.64 | $TiI_4$ dark red | $TlBr_4$ yellow |
| Zr | 40 | $Zr^{4+}$ | 2 | 8 | 18 | 8 | | | 0.87 | $ZrI_4$ brown | $ZrBr_4$ colorless |

* Color of chlorides not given since they all, except cupric chloride, are colorless.
** The $Cu^{2+}$ ion is colored blue only as the hydrate. In the anhydrous state $CuF_2$ and $CuSO_4$ are colorless and $CuCl_2$ is dark brown.

Thus, coloration of the inorganic halides is observed in those instances where the electron cloud of a heavy halide ion is greatly deformed by a cation that is capable of creating a powerful electric field, as a result of the fact that it has a small ion radius or several charges. Such salts are much less dissociated in aqueous solutions than the corresponding chlorates and nitrates. If dissociation takes place at all, as in the case of lead iodide, for example, then it is accompanied by decoloration. Additional evidence of the decrease in heteropolarity in the colored halide salts is found in their lower melting and boiling points in comparison with the other corresponding salts.

Decker [11] was the first to point out the similarity of the colored inorganic iodides to the colored ammonium iodides. Meisenheimer [17] explained the coloration of many organic and inorganic iodides by the deformation of the iodide ion by polarizing cations. Kröhnke in his articles [15] analyzed in detail the investigations carried out previously and those that he himself made in the field of the colored cycloammonium salts and expressed the opinion that the phenomenon of bathochromism in salt formation depends not only on the deformation of the anion by the cation, as in the case of AgI, but also on their redox opposition. The author pointed out that $Ag_4Fe(CN)_6$, $Ag_2SO_3$, and $AgS_2O_3$, for example, are colorless, because their anions have a low deformability. However, the salts of these same anions with the cycloammonium cations are deeply colored, since a considerable difference in oxidation-reduction potential exists between such ions.

Kröhnke first suggested that when a colored salt is formed from a cycloammonium cation and an appropriate anion one of the electrons of the anion goes over into the cation, which is thus converted into a radical depicted by structures (A) and (B).
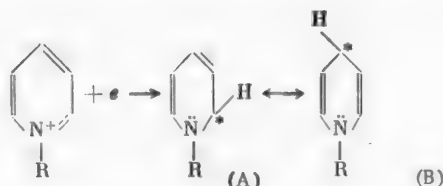


However, the author later was convinced that the pyridinium and quinolinium iodides and ferrocyanides are not paramagnetic and therefore do not contain an unpaired electron. Consequently, he arrived at the conclusion that the electron does not go over completely from the anion to the cation, but "breaks loose" and "hovers" (ist in der Schwebe) in the vicinity of the cation.

Starting with the fact that the diazonium halides contain an onium nitrogen and behave quite like the cycloammonium salts, it is logical to conclude that their color also depends on a special kind of salt bond between the diazonium cation and an easily deformed anion. The diazonium cation actually has strong electron-accepting properties, which can be considerably strengthened by the introduction into the ring of appropriate substituents. In connection with the views of Kröhnke [15] on the oxidizing character of the cycloammonium cations it should be noted that the diazonium cations also have an appreciable oxidizing potential. According to the data of Grachev [18] the oxidizing potential of 4-chlorophenyldiazonium in aqueous solution at pH 2 is +0.86, and that of 4-nitrophenyldiazonium is +0.97 v. Therefore, chlorophenyldiazonium is a stronger oxidizing agent than, for example, $Fe^{3+}$, the oxidizing potential of which is 0.75 v. Well-known examples of the oxidizing properties of diazonium compounds also are their reactions with alcohol, p-phenylenediamine, arsenous acid, and the like.

In the colored diazonium arylsulfamates of interest to us, which we have shown to have properties similar to those of the diazo iodides and bromides of Hantsch, the arylsulfamate anions occupy the place of the halogens. It must be supposed that these anions apparently also are greatly deformed by the diazonium cations. To explain the reasons for such behavior on the part of the arylsulfamate anions it is of interest to examine the data found in the literature on the diazonium salts of sulfuric acid and some of its derivatives.

As is well known, the sulfates of the diazo compounds are colorless and extremely easily soluble in water, in which they apparently are completely dissociated. The benzene- and toluenemonosulfonates differ little in color and solubility from the diazonium sulfates. However, the chloro- and nitro-substituted benzene- and toluenesulfonic acids precipitate the less soluble arylsulfonates from solutions of diazonium salts of mineral acids [19]:

$$Ar-\overset{+}{N}\equiv N|\overset{-}{X} + Ar'-SO_3H \longrightarrow Ar-\overset{+}{N}\equiv N|\overset{-}{O}_3S-Ar' + HX$$

Chloro- and nitro-substituted benzene- and toluenesulfonic acids form colorless salts with diazonium compounds of the benzene series, even those containing chloro or nitro groups. However, with tetraazobenzidine these acids yield salts of a light-yellow or yellow color. In exactly the same way, the diazonium salts of the benzene series form salts with the naphthalenemono- and disulfonic acids that are light-yellow to brownish-yellow in color.

The diazo arylsulfonates, which are characterized by considerably less explosiveness and much greater stability than the chlorides, nitrates, and sulfates, find wide application in dye technology and printing as permanent diazo salts. Apropos of them Saunders [20] writes in his monograph on the diazo compounds that ". . . their stability in the solid state is related, no doubt, to the fact that they are not ionized in this form and is also a result of their high molecular weight."

Still greater stability and depth of color characterize the products of the reaction of diazonium salts with acylamidoarylsulfonic acids that were prepared by Schroeter [21] and further investigated by us [3]. Finally, the diazonium arylsulfamates are quite deeply colored [1, 2]. The reason for the increase in the depth of color of the diazonium salts in passing from the sulfates, through the arylsulfonates and acylamidoarylsulfonates, to the arylsulfamates becomes understandable upon examining the structure of the following anions:
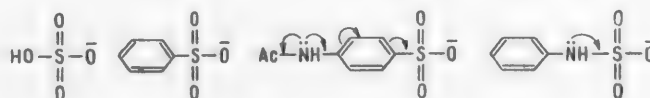


In the bisulfate (or sulfate) anion the electron cloud of the salt-forming oxygen is more stably associated with the central sulfur atom than in the arylsulfonate anion. This comes about because the second salt-forming oxygen in the sulfate ion, which has a higher affinity for electrons than the sulfur (the electronegativity of oxygen is 3.5 ev and that of sulfur is 2.5 ev [22]), draws the electrons away from the latter and makes it more positive and, consequently, more firmly bound with the electrons of the first salt-forming oxygen.

In the arylsulfonate anion the sulfur is linked with a carbon of the phenyl ring, which has the same affinity as the sulfur for electrons; therefore the sulfur becomes less positive and less firmly associated with the electrons of the salt-forming oxygen. Moreover, the phenyl ring promotes, with its sextet of $\pi$-electrons, a shift in electron density in a direction dependent on the nature of the substituent [23], in this case the sulfo group. Therefore, when the salt-forming oxygen of the arylsulfonate anion falls under the polarizing influence of a diazonium cation, it is able to give, in addition to an ionic charge, a small part of its electron cloud for greater or less intrusion into the electron gap of the cation. In the final analysis, the heteropolarity of the bond between the cation and the anion decreases, which leads to a decrease in solubility and dissociation of the diazonium arylsulfonate formed in comparison with the corresponding sulfate and in certain cases even results in a slight deepening of the color.

In the acylamidoarylsulfonate anion the nitrogen of the amido group has a pair of solitary electrons, therefore the shift in electron density toward the salt-forming oxygen is naturally more considerable than in the arylsulfonate anion and the intrusion of the electron cloud of the anion into the electron gap of the diazonium cation becomes greater. As a result, the coloration of the diazonium acylamidoacylsulfonates is deeper than that of the arylsulfonates. At the same time it should be noted that the shift of the free electron pair of the amido group in the direction of the sulfo group is partially hindered by the electron-accepting acyl group that is bound with the amido group. The more "acid" the acyl radical, the stronger is the shift in the opposite direction. A hypsochromic effect of corresponding intensity is the result of this. On the other hand, replacement of the phenyl ring by a naphthyl group in the acylamidoarylsulfonate anion leads to a bathochromic effect for the same reasons that this occurs in ordinary dyes.

It can be easily understood that in the arylsulfamate anion the shift of the free pair of electrons of the amido group toward the salt-forming oxygen is considerably greater than in the acylamidoarylsulfonate anion. In this case the mechanism for "pulling" the electron cloud of this oxygen into the electron gap of the diazonium cation is more completely exhibited, as a result of which the diazonium arylsulfamates are more deeply colored than the corresponding acylamidoarylsulfonates.
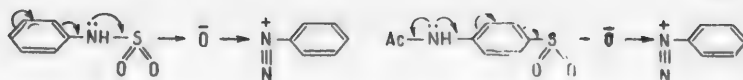
In complete agreement with the above discussion is the fact that the more electron-accepting substituents there are in the phenyl ring, the more considerable is the electron deficiency on the onium nitrogen and, consequently, the deeper is the color of such a diazonium arylsulfamate or acylamidoarylsulfonate.

We think that the phenomenon of bathochromism as a result of salt formation of a special type is rather similar to the phenomena of bathochromism as a result of intermolecular electron interaction of the donor-acceptor type, to which numerous investigators are devoting more and more attention [24, 25]. Of these investigations, the closest to the problem studied by us are the ones concerned with the study of the reaction of dipyridylium and quinolinium salts with amines.

Emmert [26] showed that N,N'-dimethyl-$\gamma$,$\gamma$'-dipyridylium chloride forms colored molecular compounds with aromatic diamines. Mikhailenko and Minof'ev [27] observed the appearance of color when benzylquinolinium chloride was reacted with monoamines (aniline, p-toluidine, and diphenylamine), but attributed it to the cleavage of the heterocycle with the formation of polymethine dyes. However, Vompe [28] and Izmail'skii [29] showed that in this instance molecular complexes are formed.

In all these cases the quaternary cycloammonium group is considered, like the nitro group, as an acceptor and the arylamine as a donor of electrons [29]. However, in contrast to the nitro group, the quaternary cycloammonium group is a cation. Therefore it is more proper to suggest that in this instance the cation is attracted not to the whole arylamine molecule, as is observed in complex formation between nitro compounds and aromatic hydrocarbons or amines, but particularly to the nitrogen of the amino group, which has an unshared electron pair.
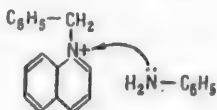


Still more localized is the interaction of a cycloammonium or diazonium cation with an arylsulfamate or acylamidoarylsulfonate anion or with a heavy halide anion. In the crystal lattice of the solid salt formed in this instance the two ions are drawn together, naturally, to a distance usual for an ionic bond. Such a close approach is intensified by the process of partial "pulling in" of the electron cloud from the salt-forming oxygen of the sulfo group by the onium nitrogen, which has an additional electron deficiency because of the electrophilic substituents in the benzene ring. If in this process the density of such an electron cloud is significantly increased because of the electron-donor properties of the amino group, the aryl group, and the substituents on the aryl group, then the salt acquires color. Upon solution of such a colored salt in water it dissociates into ions, which in this case are hydrated. Under these conditions, the more dilute the aqueous solution the more the donor-acceptor mechanism between the cation and anion is disturbed, and the color of the salt is weakened or entirely disappears.

## SUMMARY

1. Evidence has been brought forward that the diazo bromides, thiocyanates, and iodides whose color Hantzsch explained on the basis of their syn-diazo structure are actually diazonium salts.

2. The similarity in properties of the diazonium bromides, thiocyanates, and iodides with the diazonium arylsulfamates and acylamidoarylsulfonates has been established.

3. It has been suggested that the arylsulfamate and acylamidoarylsulfonate anions have electron-donor properties that are characteristic also of the bromide, thiocyanate, and iodide anions, and that this general property is the cause of the coloration of the corresponding series of diazonium salts.

4. The similarity of a number of properties of the colored diazonium arylsulfamates, acylamidoarylsulfonates, bromides, thiocyanates, and iodides to the colored bromides, thiocyanates, and iodides of quaternary ammonium bases containing nitrogen in the heterocycle (pyridinium, quinolinium, etc.) has been demonstrated. The

opinion has been expressed that the cause of the color of the series of salts enumerated is the presence in them of an onium nitrogen that has an increased electron deficiency as a result of electron-acceptor substituents in the aryl rings linked with this nitrogen.

5. An explanation has been suggested of the reason for the formation of colored salts from colorless diazonium cations or ammonium cations of nitrogen-containing heterocycles on the one hand, and anions of heavy halides, arylsulfamic and acylamidoarylsulfonic acids on the other hand, as a result of a special donor-acceptor electron interaction between the ions, which supplements the usual salt bond.

6. The similarity and the difference between the donor-acceptor electron interaction of the ions in the colored salts enumerated above and the donor-acceptor interaction of the intermolecular type has been discussed.

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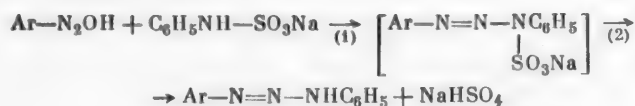
# REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

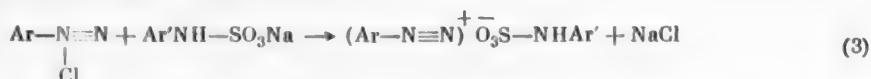## XII. DIARYLTRIAZENE-N-SULFONIC ACIDS AND THEIR DIAZONIUM SALTS

### D. Z. Zavel'skii and L. A. Lishnevskaia

In one of our communications [1] it has been shown that diazo compounds are capable of entering into a diazoamino condensation with phenylsulfamic acid. When this occurred, however, it appeared that the diaryltriazene-N-sulfonates that apparently were formed in the initial phase were capable under the conditions of the diazoamino condensation reaction, i. e., at pH ~ 6 and room temperature, of splitting out their sulfo group and being converted to mixed diaryltriazenes

$$\text{Ar--N}_2\text{OH} + \text{C}_6\text{H}_5\text{NH--SO}_3\text{Na} \xrightarrow{(1)} \left[ \begin{array}{c} \text{Ar--N=N--NC}_6\text{H}_5 \\ | \\ \text{SO}_3\text{Na} \end{array} \right] \xrightarrow{(2)}$$

$$\rightarrow \text{Ar--N=N--NHC}_6\text{H}_5 + \text{NaHSO}_4$$

In the experiments on diazoamino condensation carried out at that time we aimed for disappearance of the reaction for the active diazo compound, which lasted for a rather long time.

Further investigations have shown that the diazoamino condensation (1) proceeds for not more than 20-30 min, but the reaction of splitting out the sulfo group (2) proceeds considerably more slowly. We were able to utilize this circumstance for the synthesis of the diaryltriazene-N-sulfonates sought and for a study of their interesting properties.

It was established that when a solution of a diazo compound with a pH value of 3 is mixed with a solution of a phenyl- or 4-tolylsulfamate in a buffer of pH 6, during the first moments the brightly colored and rather poorly soluble diazonium salt of the arylsulfamic acid is formed [2].

$$\text{Ar--N=N} + \text{Ar'NH--SO}_3\text{Na} \longrightarrow (\text{Ar--N=N})^+ \overset{-}{\text{O}}_3\text{S--NHAr'} + \text{NaCl} \tag{3}$$
$$|$$
$$\text{Cl}$$

Then in the course of 15-30 min a sharp weakening of the color of the reaction suspension takes place as a result of the conversion of this salt to a new, considerably more highly colored compound, poorly soluble in water and extremely unstable, which proved to be the diaryltriazene-N-sulfonate. When such electrophilically substituted diazo compounds as 2,5-dichloro- or 4-nitrodiazobenzene are used, isolation of the diaryltriazene-N-sulfonates obtained from them requires special precautions to avoid decomposition of the latter. The whole reaction suspension has to be poured in a thin layer onto unfired clay plates.* In this way the mother liquor is quickly drawn off by the pores of the plate and the compound is removed as an almost dry layer, which is additionally dried for a half-hour in vacuo over potassium hydroxide. The compounds obtained are so unstable that the whole process of their synthesis and isolation must not take more than 1 hr. When they are kept even in dry form, their crystalline structure and color rapidly change, and they split out their sulfo group. The diaryltriazene-N-sulfonate obtained from 4-chlorodiazobenzene and phenylsulfamic acid is somewhat more stable. It is possible to isolate it by simple filtration and it can be kept for 1-2 days.

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* Before use it is expedient to bake the plates thoroughly and to keep them in a desiccator over some dehydrating agent.

The condensation products of diazo compounds with arylsulfamic acids when exposed in the dry state to the incandescent wire of an electric heater burst into flames instantaneously, and their aqueous suspension combines in neutral medium with any azo components. This forces us to suggest that they contain an active diazo group. However, it further appears that when the new compounds are mixed with an excess of a titrated solution of β-naphthol at pH 7 they actually absorb 1 equivalent of the naphthol in 10 min, but when the reaction is continued further, an additional, much slower absorption of β-naphthol occurs that reaches a maximum of 2 equivalents in 5-6 hrs. Consequently, the compounds under investigation contain two diazo groups, one of which is considerably more active than the other.

The new compound can be dissolved in concentrated hydrochloric acid. If nitrite is added to the hydrochloric acid solution, after a short delay the excess nitrous acid is removed by the addition of sulfamic acid, and after that the mixture is treated with excess β-naphthol at an appropriate pH, then 3 equivalents of β-naphthol are used up in the combination. From this it follows that the molecule of the new compound contains one amino group in addition to the two diazo groups.

On the basis of the properties described above we have proposed structure (A) for the new compounds.
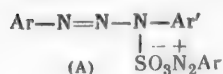
$$Ar—N=N—N—Ar'$$
$$\underset{(A)}{\overset{|}{\quad}}\ \overset{-\ +}{SO_3N_2Ar}$$

Actually, the diazonium salt of the diaryltriazene-N-sulfonic acid has one active salt-forming diazo group and another bound with the imido group of the arylsulfamic acid in a diazoamino compound. Upon coupling with β-naphthol in neutral medium, the condensation product, for example, of 2,5-dichlorodiazobenzene with 4-tolylsulfamic acid, will react in the following way:



(4)



(5)
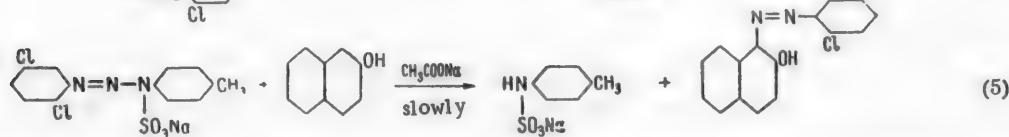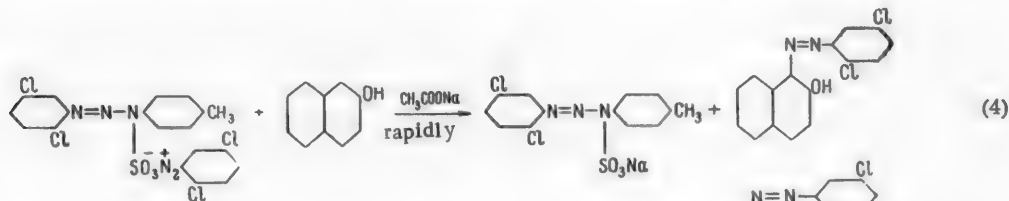
Investigation has confirmed that a product of both reactions (4) and (5) is 2,5-dichlorophenylazo-β-naphthol, which was isolated and identified with the corresponding specially synthesized azo dye.

It was shown that the solution remaining after coupling of the compound under investigation with β-naphthol in neutral medium and the removal of the azo dye by filtration contains sodium tolylsulfamate, since it absorbs nitrite in acid medium, and after this it couples with β-naphthol to form 4-tolylazo-2-naphthol. The latter was also demonstrated by identification with the same specially synthesized azo dye.



(6)



(7)
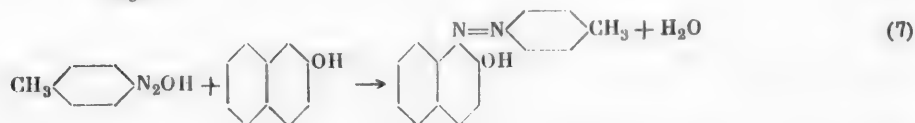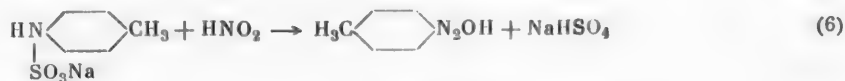
Exactly the same results were obtained in the investigation of the condensation products of 2,5-dichlorodiazobenzene with phenylsulfamic acid and also of 4-nitrodiazobenzene, 3-nitrodiazobenzene, and 4-chlorodiazobenzene with phenyl- and tolylsulfamic acids. The structural formulas of these compounds, which were additionally confirmed by quantitative analyses for diazo nitrogen and sulfur, are given below.

(I)    (II)    (III)

(IV)    (V)    (VI)
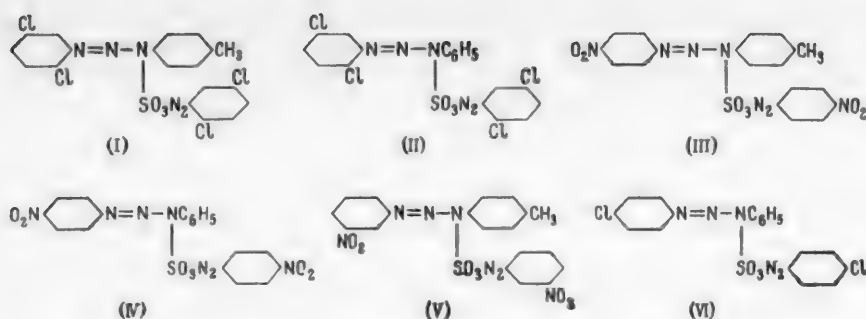
Thus it was possible to show that the arylsulfamic acid actually condenses with the diazo compounds to form diaryltriazene-N-sulfonic acids, which precipitate out as diazonium salts as a result of the poor solubility of the latter. In this process, the brightly colored diazonium salts of the arylsulfamic acids at first are formed according to reaction (3), and then these salts enter into a diazoamino condensation with a second molecule of the diazo compound.

$$Ar-N\equiv N]^+\ ^-O_3S-NHAr' + ArN_2OH \longrightarrow Ar-N\equiv N]^+\ ^-O_3S-\underset{\underset{N=N-Ar}{|}}{N}-Ar' + H_2O \tag{8}$$
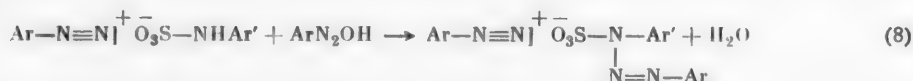
It has already been mentioned that in this new series of compounds, which for brevity we call diazoamino-diazo salts, the salt-forming diazo group enters into azo-combination in neutral medium, and that this combination is completed in 10 min (4). It is a new and unexpected observation that the second diazo group, which is bound in the form of a diazoamino compound, also enters into azo-combination in neutral medium, although much more slowly in 5-6 hrs (5). But it is known that ordinary diazoamino compounds, which are soluble in water, can split out their diazo component only in more or less acid media, and precisely this property has made it possible to use the diazoamino compounds mixed with the naphthols of the AS series (azotols) for color printing of fabrics [3, 4].

$$Ar-N=N-N-CH_3$$
$$\underset{SO_3\ ^-N_2^+-Ar}{|}$$
(B)

We have previously synthesized the diazo salts of methyltriazene-N-sulfonic acid by mixing diazo salts with methylsulfamic acid at pH 3. For these salts we proved the general structural formula (B) [5].
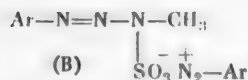
However, in these compounds only the salt-forming diazo component was capable of azo-coupling in neutral medium, and the second diazo component, covalently bound with the amino group, was split out only upon acidification. Comparison of the ability of the diazo salts of methylaryltriazene- and diaryltriazenesulfonic acids to couple in neutral medium has compelled us to suggest that either the structural formula proposed by us for the latter is incorrect, or replacement of the methyl group by an aryl group in compounds of this type results in strong polarization and weakening of the bond between the diazo group and the imido group.

A solution of the question arising could be arrived at by the synthesis, instead of the diazo compounds, of the simpler and therefore more easily investigated sodium salts of the diaryltriazene-N-sulfonic acids, the properties of which could be compared directly with those of the potassium salts of the methylaryltriazene-N-sulfonic acids that have been thoroughly studied by us previously.

It appeared that all six of the diazo salts of diaryltriazene-N-sulfonic acids synthesized by us, which were poorly soluble in water, dissolved readily in 0.1 N sodium hydroxide solution. Moreover, replacement of the diazo cation by the sodium cation evidently occurs with simultaneous conversion of the diazo cation to isodiazotate (in the case of 2,5-dichloro- or 4-nitrodiazobenzene).
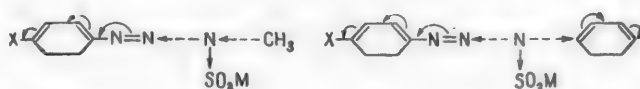
$$Ar-N=N-N-Ar' + NaOH \longrightarrow Ar-N=N-N-Ar' + Ar-N-NO \tag{9}$$
$$\underset{SO_3N_2Ar}{|} \qquad\qquad \underset{SO_3Na}{|} \qquad \underset{Na}{|}$$
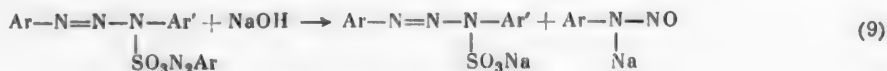
However, isolation of the sodium salts from the diazoaminodiazo salts synthesized from 2,5-dichloro- or 4-nitrodiazobenzene in a form sufficiently pure for the purposes of the investigation proved to be difficult because of their instability. Only by the action of alkali on the 4-chlorophenyldiazonium salt of 4-chlorodiphenyltriazene-N-sulfonic acid (VI) did we succeed in separating the corresponding sodium salt (VII), the structure of which was exactly established by analyses for diazo nitrogen, sulfur, sodium, and for diazo- and amino-group content, and also by conversion to the original diazoaminodiazo salt (VI) by the action of 4-chlorophenyldiazonium chloride on the sodium salt.

$$Cl\langle\quad\rangle N\!=\!N\!-\!NC_6H_5 + Cl\langle\quad\rangle N_2Cl \longrightarrow$$
$$(VII) \qquad SO_3Na$$
$$\longrightarrow Cl\langle\quad\rangle N\!=\!N\!-\!NC_6H_5$$
$$SO_3N_2\langle\quad\rangle Cl + NaCl$$
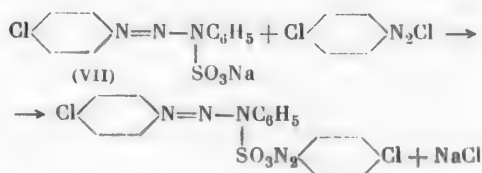
It was confirmed that sodium 4-chlorodiphenyltriazene-N-sulfonate actually is capable of azo-coupling in neutral medium. More than that, it retains the ability to couple in bicarbonate, sodium carbonate, and even caustic alkali medium. Only when the concentration of sodium hydroxide reaches 28-30% does coupling not occur. At the same time, the structurally similar potassium salts of the methylaryltriazene-N-sulfonic acids combine with azo constituents at room temperature only in acid media with pH 2-4 [6]. Consequently, it can be considered clear that just the replacement of the methyl group by an aryl group in these compounds leads to weakening of the bond between the diazo and the amino groups.

Examining the structure of the methylaryl- and the diaryltriazene-N-sulfonates, we apparently can come to the following conclusion.

$$X\langle\quad\rangle N\!=\!N\!\leftarrow\!-\!-N\!\leftarrow\!-\!-CH_3 \qquad X\langle\quad\rangle N\!=\!N\!\leftarrow\!-\!-N\!-\!-\!\rightarrow\langle\quad\rangle$$
$$SO_3M \qquad\qquad SO_3M$$

In the methylaryltriazene-N-sulfonates the bond between the diazo nitrogen and the amino group is weakened as a result of a shift in electron density in the direction of the electrophilic arylazo group and the sulfo group. However, the electron-donor methyl group, which increases the electron density of the imido nitrogen, thus strengthens the bond between the nitrogen and the diazo group. If, however, an aryl group appears in place of the methyl group in the same position, then it, having an electrophilic character, not only does not strengthen, but even weakens the bond of the imido nitrogen with the diazo group.

In our preceding communications [2, 7, 8] we have shown that the diazonium salts of the arylsulfamic acids, in contrast to most of the other diazonium salts, are deeply colored; moreover, the more electrophilic the substituents in the benzene ring of the diazo cation and the more nucleophilic the substituents in the benzene ring of

$$X\langle\quad\rangle N\!=\!N\!-\!N\!-\!\langle\quad\rangle Y$$
$$SO_3N\!-\!\langle\quad\rangle X$$
$$(C) \qquad N$$
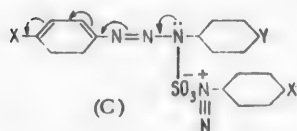
the arylsulfamate anion, the deeper is the color of the salts. The diazonium salts of the diaryltriazene-N-sulfonic acids described in the present work can also be considered as salts of arylsulfamic acids in which a nitrogen has been replaced by an arylazo group (C). Therefore, it might seem that we could expect them also to be deeply and intensely colored. Actually all these salts are colored, weakly or highly, from cream to mustard or light brown.

The apparent contradiction can be easily explained by the fact that in these salts the imido group of the arylsulfamate ions is replaced by the strongly electrophilic arylazo groups, in which there are also electrophilic substituents ($X = NO_2$, and the like). As a result of this, the unshared electron pair on the nitrogen of the arylsulfamic acid cannot transmit to the oxygen of the sulfo group the additional electron density necessary to create the special type of salt bond with the diazonium cation that provides the strong bathochromic effect.

## EXPERIMENTAL

2,5-Dichlorophenyldiazonium salt of 2,5-dichloro-4'-methyldiphenyltriazene-N-sulfonic acid (I). 1.62 g of 2,5-dichloroaniline was dissolved in 6 ml of 5 N hydrochloric acid, cooled to 0°, and diazotized with a small

excess of 5 N nitrite solution. To the diazo solution obtained were added a few crystals of sulfamic acid to remove the excess nitrous acid, and then sodium acetate until a pH of 3 was reached. The solution was filtered and kept in ice.

2.3 g of sodium 4-tolylsulfamate was dissolved in water and 40 ml of concentrated acetate buffer with a pH of 6 was run in. Into the cooled solution, from which the tolylsulfamate began to precipitate, was poured the diazo solution, with stirring at 0°. The reaction suspension immediately became red and in 3-5 min it was filled with red crystals of the 2,5-dichlorophenyldiazonium 4-tolylsulfamate, which upon further stirring began to lose their form and color. In 15-20 min, when the mixture lost its rosy hue and took on a creamy color, stirring was stopped and the reaction suspension was poured in a thin layer onto plates of unfired clay. After remaining on the plates for 40 min the layer of light cream-colored material was removed with a knife. When kept longer, the product began to turn brown, which indicated the start    of decomposition. The powder was further dried in a vacuum desiccator painted with black lacquer, over potassium hydroxide. 2.3-2.6 g of the diazonium salt was obtained (80.8-91.3%). Isolation of the reaction product by ordinary filtration and drying, or delay in the process of preparation and isolation, led to its turning brown and  partially decomposing.

The diazoaminodiazo salt was extremely unstable on storage. We did not succeed in recrystallizing it, because it was poorly soluble in water and decomposed in organic solvents. However, when the conditions described above were maintained, the product was obtained sufficiently pure for analysis, but the analysis had to be carried out immediately after drying. If the diazoaminodiazo salt was not affected by decomposition, it dissolved completely in the cold in 0.1 N sodium hydroxide solution with a pale yellow coloration. By addition of acetic acid to the alkaline solution the diazoaminodiazo salt could again be precipitated. When the dry product, on the end of a spatula, was brought close to an incandescent electric coil, it immediately burst into flames. The diazoaminodiazo salt that had decomposed on storage gave off sulfuric acid, detectable by the acid reaction to Congo paper and the formation of a precipitate with barium chloride. The suspension of the diazoaminodiazo salt in water actively combined with azo constituents in neutral medium.

Found %: S 5.60, 5.56;  diazo nitrogen 9.56, 9.82. $C_{19}H_{13}O_3N_5SCl_4 \cdot 2H_2O$. Calculated %: S 5.63; diazo nitrogen 9.84.

Coupling of diazoaminodiazo salt with β-naphthol in neutral medium. a) 0.5984 g of the compound was stirred with 50 ml of 0.1 N β-naphthol solution at room temperature for 10 min. The β-naphthol solution was previously neutralized with acetic acid to pH 7. The excess β-naphthol was titrated with a 0.1 N p-nitrophenyldiazonium solution immediately after the 10 min combination period.

The actual consumption of 0.1 N β-naphthol solution was 10.88 ml $C_{19}H_{13}O_3N_5SCl_4 \cdot 2H_2O$. The calculated consumption of 0.1 N β-naphthol, based on monoequivalence of the compound, was 10.51 ml.

b) 0.5169 g of the compound was coupled with an excess of β-naphthol under the same conditions, but for a period of 2 hrs. The consumption of 0.1 N β-naphthol solution was 13.28 ml. The calculated consumption based on monoequivalence of the compound, was 9.08 ml.

c) 0.2386 g of the compound was coupled with β-naphthol under similar conditions for a period of 6 hrs. The actual consumption of 0.1 N β-naphthol solution was 8.23 ml. The calculated consumption, based on biequivalence of the compound, was 8.38 ml.

Determination of the total content of two diazo and one amino components. A weighed portion of the diazoaminodiazo salt was dissolved in 50 ml of 0.1 N sodium hydroxide, 0.3 g of sodium nitrite was added, and the solution obtained was poured into a mixture of 5 ml of 5 N hydrochloric acid and ice. After 5 minutes' stirring, 50 ml of 0.1 N β-naphthol solution was run into the solution, its pH was brought to 7 with bicarbonate solution, and after 30 minutes' stirring the excess of β-naphthol was determined with 0.1 N p-nitrophenyldiazonium solution.

0.5431 g of compound required 27.65 ml of 0.1 N β-naphthol. $C_{19}H_{13}O_3N_5SCl_4 \cdot 2H_2O$. Calculated, 28.62 ml of 0.1 N β-naphthol (if the compound is considered triequivalent).

0.4879 g of compound required 26.18 ml of 0.1 N β-naphthol. Calculated, 25.71 ml of 0.1 N β-naphthol.

Qualitative determination of salt-forming diazo compound. 1.3 g of the diazoaminodiazo salt was poured into 50 ml of 0.1 N β-naphthol solution, which had been brought to a pH of 7 with acetic acid, and 100 ml of

water and stirred vigorously for 10 min. The red azo dye that separated out was filtered off and the precipitate was washed with warm 0.1 N sodium hydroxide solution, and then with water. After drying and one recrystallization from glacial acetic acid the azo dye melted at 183°. The azo dye specially synthesized from 2,5-dichlorophenyldiazonium and β-naphthol also melted at 183° [9] and when mixed with the dye obtained from the diazoaminodiazo salt it melted without depression.

Qualitative determination of salt-forming diazo components and of the diazo group linked with amino components. 0.8 g of the diazoaminodiazo salt was coupled with β-naphthol at pH 7 for 6 hrs with stirring. After standing overnight, the azo dye that had precipitated was separated as described above. In this case also 2,5-dichlorophenylazo-β-naphthol was obtained with m. p. 183°. Consequently, both azo groups were 2,5-dichlorodiazobenzene groups.

Determination of amino components. 2.0011 g of the diazoaminodiazo salt was coupled with an excess of β-naphthol at pH 7 for 6 hrs. The next day the suspension was acidified and the azo dye that precipitated was filtered off, together with a small amount of β-naphthol that settled out. The filtrate, after addition of 5 ml of concentrated hydrochloric acid, was titrated with 0.1 N nitrite solution. Consumption was 19.36 ml, or 55.1% of the calculated amount.

The solution titrated with nitrite was neutralized with sodium carbonate and poured into an excess of alkaline β-naphthol solution. The azo dye that precipitated was washed with water, dried, and recrystallized twice from glacial acetic acid, after which it melted at 129.0-129.5°. The m. p. of 4-tolylazo-β-naphthol is 130° [9]. Consequently, the amino component was 4-tolylsulfamic acid.

2,5-Dichlorophenyldiazonium salt of 2,5-dichlorodiphenyltriazene-N-sulfonic acid (II). 1.95 g of sodium phenylsulfamate was dissolved in 30 ml of water and mixed with 75 ml of concentrated acetate buffer with pH 6. Then a 0.01 M solution of 2,5-dichlorodiazobenzene prepared as described above was run in with stirring. Immediately a bright orange precipitate of 2,5-dichlorophenyldiazonium phenylsulfamate separated out, which upon further stirring for 30-40 min gradually disappeared, being converted into pale yellow crystals that had the appearance under a microscope of voluminous flakes gathered into rosettes. As soon as the orange crystals disappeared, the reaction mass was poured in a thin layer onto unglazed porcelain plates and after 30-40 minutes' delay the almost dry material was removed with a knife and further dried for 20 min in a vacuum desiccator over solid potassium hydroxide. Yield 2.1-2.3 g (about 80%).

The diazoaminodiazo salt obtained was poorly soluble in water and decomposed in organic solvents. In 0.1 N alkali solution it formed a clear, pale yellow solution that slowly combined with H acid. If the product was not fully soluble in alkali, this was an indication of its partial decomposition.

When the diazoaminodiazo salt was separated by filtration and washing with glacial acetic acid, with subsequent drying on unglazed porcelain, the compound became yellow, then turned brown and was converted into a paste that was acid to Congo, insoluble in water, poorly soluble in sodium hydroxide, and contained the sulfate ion.

The dry diazoaminodiazo salt when brought close to an incandescent electric coil instantly burst into flames.

Found %: diazo nitrogen 9.90. $C_{18}H_{11}O_3N_5SCl_4 \cdot 2H_2O$. Calculated %: diazo nitrogen 10.09.

Determination of total content of diazo components. 0.3203 g of compound was stirred with 20 ml of 5 N hydrochloric acid at 0° for 1 hr. Into the pale yellow, almost transparent, solution that was obtained was poured 25 ml of 0.1 N β-naphthol solution, bicarbonate was added carefully to bring the pH to 7, and, after 30 minutes' stirring, the excess β-naphthol was titrated with 0.1 N solution of p-nitrophenyldiazonium.

Actual consumption of 0.1 N β-naphthol solution was 11.35 ml, calculated 11.54 ml.

Determination of the total of the diazo components and the amino components. 0.1882 g of compound was stirred with 20 ml of 5 N hydrochloric acid at 0° for 1 hr until the material dissolved, an excess of nitrite was added, and after 15 minutes' stirring the excess nitrous acid was removed by the addition of sulfamic acid. The solution of diazo compounds obtained was coupled with an excess of 0.1 N β-naphthol solution, first at pH 7 and finally at pH 9-10.

Actual consumption of 0.1 N β-naphthol solution was 9.97 ml, calculated (based on triequivalence of the compound) 10.17 ml.

4-Nitrophenyldiazonium salt of 4-nitrodiphenyltriazene-N-sulfonic acid (IV). To a solution of 1 g of sodium phenylsulfamate in 25 ml of concentrated acetate buffer with pH 6, cooled in ice, was added 0.005 mmoles of p-nitrophenyldiazonium that had been freed of excess nitrous acid and adjusted to pH 3 with acetate.

Immediately the red-brown 4-nitrophenyldiazonium salt of phenylsulfamic acid precipitated, which upon further stirring gradually started to lose its color and brilliance. When the material was observed under a microscope, it could be seen that there were fine yellow crystals along with the large rose-colored platelets of the diazo salt.

30 min after the start of the reaction the mixture was poured in a thin layer onto unglazed clay plates. In 30-35 min the material was easily poured from the plates as a dry, light brown powder.

The diazoaminodiazo salt was poorly soluble in water, but a suspension combined vigorously with H acid. It was completely soluble in 0.1 N alkali solution, forming a clear red solution. Upon heating over an electric heater the salt instantly burst into flames.

Analysis for the total diazo components and amino components. 0.2509 g of compound was dissolved in 20 ml of 5 N hydrochloric acid cooled with ice. The reddish solution formed was diazotized with an excess of nitrite. In 10 min the excess nitrite was removed by the addition of sulfamic acid and the solution was poured into 25 ml of 0.1 N $\beta$-naphthol solution. The pH of the reaction mixture was adjusted to 7 with bicarbonate and the excess $\beta$-naphthol was titrated with 0.1 N p-nitrophenyldiazonium solution.

Actual consumption of 0.1 N $\beta$-naphthol solution was 15.92 ml, calculated (based on triequivalence of the compound) 15.96 ml.

4-Nitrophenyldiazonium salt of 4-nitro-4'-methyldiphenyltriazenesulfonic acid (III). The diazoamino-diazo salt was prepared from 4-nitrophenyldiazonium and 4-tolylsulfamic acid at pH 6 under conditions similar to those described above. The mustard-colored salt was poorly soluble in water, but a suspension combined vigorously with H acid. It dissolved completely in 0.1 N sodium hydroxide solution with the formation of a clear red solution. It also was soluble in 5 N hydrochloric acid, forming a clear, pale yellowish solution that contained 2 moles of p-nitrodiazobenzene and 1 mole of p-toluidine.

3-Nitrophenyldiazonium salt of 3-nitro-4'-methylphenyltriazene-N-sulfonic acid (V). This compound was prepared under the same conditions as the 4-nitro derivative. The salt was cream-colored. It was poorly soluble in water. An aqueous suspension combined well with azo components. In the dry state, when it was placed on the end of a spatula and brought close to the incandescent coil of an electric heater, it flared up strongly. In 0.1 N alkali it formed a clear yellow solution. It dissolved completely in 5 N hydrochloric acid with the formation of an almost colorless solution containing 2 moles of 3-nitrodiazobenzene and 1 mole of p-toluidine.

4-Chlorophenyldiazonium salt of 4-chlorodiphenyltriazene-N-sulfonic acid (VI). 2.55 g of 4-chloroaniline was diazotized as usual, the excess of nitrous acid was removed with sulfamic acid, and sodium acetate was added to bring the pH to 3. The diazo solution was filtered and kept in ice.

4.3 g of sodium phenylsulfamate was dissolved in 20 ml of water, 30 ml of saturated sodium bicarbonate solution was added, and the mixture was cooled with ice. Into the solution produced was poured a cold solution of 4-chlorophenyldiazonium, with stirring. Thereupon, a light yellow precipitate immediately appeared, but there also was noticeable on the bottom and sides of the reaction beaker a pasty, orange-yellow mass of 4-chloro-phenyldiazonium phenylsulfamate, which was gradually converted to a light yellow precipitate on stirring. After 1.5 hrs stirring at 0° the reaction mass, which had become homogeneous, was filtered. The precipitate was washed 5 times with 10-15 ml portions of ice water, transferred to an unglazed porcelain plate, pressed out, and dried overnight in a darkened vacuum desiccator over solid potassium hydroxide. The light yellow powder (fine crystals under the microscope) that was obtained weighed 3.7 g (82.2%). It was poorly soluble in cold water. It dissolved in alcohol and acetone with a yellow color, and was insoluble in benzene and chloroform. The aqueous, alcoholic, and acetone solutions combined with azo components. The solution in acetone deposited in a few minutes a new, weakly colored, flocculent product, which was not investigated.

Found %: diazo nitrogen 12.33; S 6.96. $C_{18}H_{13}O_3N_5SCl_2$. Calculated %: diazo nitrogen 12.44; S 7.12.

## Analysis for Combination at pH 7

a) Coupling in 10 min. 0.4522 g of compound: 9.6 ml 0.1 N $\beta$-naphthol. $C_{18}H_{15}O_3N_5SCl_2$. Calculated: 10.04 ml 0.1 N $\beta$-naphthol solution (if the compound is considered monoequivalent).

b) Coupling in 6 hrs. 0.4778 g compound: 19.9 ml 0.1 N $\beta$-naphthol. $C_{18}H_{13}O_3N_5SCl_2$. Calculated: 21.2 ml 0.1 N $\beta$-naphthol (if the compound is considered biequivalent).

Sodium salt of 4-chlorodiphenyltriazene-N-sulfonic acid (VII). 2 g of 4-chlorophenyldiazonium salt of 4-chlorophenyltriazene-N-sulfonic acid was dissolved in 40 ml of 0.5 N sodium hydroxide solution at 8°. The compound dissolved almost completely. The filtered orange solution became turbid in the suction flask because the sodium salt started to precipitate. 10 ml of saturated sodium acetate solution was added to the filtrate and it was placed in ice. The precipitate that separated out (light yellow needles under the microscope) was filtered off, washed with several milliliters of ice water, pressed out on an unglazed porcelain plate, and dried in a vacuum desiccator over potassium hydroxide overnight. The dry beige-colored precipitate weighed 0.89 g (54.3%).

The sodium salt of the triazene-N-sulfonic acid was slightly soluble in water (yellow solution). When the aqueous solution stood at room temperature it gradually turned brown, and when heated, it vigorously gave off gas like a solution of an azo compound. The triazene-N-sulfonate solution combined with H acid to form an azo dye not only in acetic acid medium, but also in bicarbonate and sodium carbonate media. The combination still occurred in 0.5 N alkali solution, but ceased in 28-30% solution; however, when bicarbonate was added to the alkali solution, i. e., on conversion to a sodium carbonate medium, combination again was resumed.

The triazene-N-sulfonate was readily soluble in alcohol (the solution was the color of strong tea), and only a little less so in ether (with the same color). The product was slightly soluble in chloroform and insoluble in benzene and petroleum ether.

The dry sodium salt decomposed instantly over an incandescent coil of an electric heater with the evolution of yellow vapors but without fire.

When a solution of 4-chlorophenyldiazonium chloride, neutralized with bicarbonate, was added to an aqueous solution of the sodium salt of 4-chlorodiphenyltriazine-N-sulfonic acid, a light yellow precipitate of the above-described 4-chlorophenyldiazonium 4-chlorodiphenyltriazene-N-sulfonate immediately separated out. When alkali was added to this suspension, a solution of the sodium salt again was formed.

Found %: diazo nitrogen 7.26, 7.43; S 8.47; Na 6.38. $C_{12}H_9O_3N_3SClNa$. Calculated %: diazo nitrogen 7.57; S 8.67; Na 6.22.

Analysis for combination with $\beta$-naphthol. 0.4814 g of compound was dissolved in 100 ml of water, 25.0 ml of 0.1 N $\beta$-naphthol adjusted to a pH 7 with acetic acid was added, and the mixture was stirred for 2 hrs at room temperature and left overnight. In the morning the excess $\beta$-naphthol was titrated with 0.1 N p-nitrophenyldiazonium solution. Consumption of 0.1 N $\beta$-naphthol was 13.44 ml; calculated consumption for $C_{12}H_9O_3N_3SClNa$ was 13.02 ml.

Analysis for phenylsulfamic acid. After combination with $\beta$-naphthol the precipitate of azo dye was filtered off and washed. To the filtrate and wash water was added 5 ml of concentrated hydrochloric acid and the mixture was titrated with 0.1 N sodium nitrite solution. 13.23 ml was consumed; calculated consumption for $C_{12}H_9O_3N_3SClNa$ was 13.02 ml.

### SUMMARY

1. By the action of diazonium salts on arylsulfamic acids, diazonium salts of diaryltriazene-N-sulfonic

acids $\text{Ar—N=N—N}\begin{smallmatrix} \diagup \text{Ar'} \\ \diagdown \text{SO}_3\text{N}_2\text{—Ar'} \end{smallmatrix}$ , have been synthesized, the structure of the latter salts has been demonstrated, and some of their properties have been studied.

2. It has been established that it is possible to prepare from the diazonium salts of the diaryltriazene-N-sulfonic acids by the action of alkali the corresponding alkali salts, which can again be converted to the starting diazonium salts by exchange decomposition with diazonium chlorides.

3. It has been shown that in contrast to the methylaryltriazene-N-sulfonates and other triazenes of similar structure, in the diaryltriazene-N-sulfonates the diazo component is linked with the imido group so unstably that it is capable of splitting out and combining with azo components in neutral and even in alkaline media. An explanation of this property has been suggested.

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# INVESTIGATIONS IN THE FIELD OF ORGANOCYCLOSILOXANES

## III. THE USE OF THE METHOD OF THERMOOXIDATIVE DESTRUCTION FOR THE INVESTIGATION OF THE HYDROLYSIS PRODUCTS OF ALKYLTRICHLOROSILANES

### N. N. Sokolov

As a result of the complete hydrolysis of difunctional organosilicon monomers, linear and cyclic organopolysiloxanes are obtained in various ratios. The problem of the structure of polymers formed as a result of the hydrolysis of monomers which are more than difunctional is more complicated.

As a result of the hydrolysis of trifunctional monomers in excess water, complex spatial polymers with the empirical formula $(RSiO_{1.5})_n$ are formed. In this instance the number of blocking groups is markedly reduced and the isolation of the individual hydrolysis products is very difficult.

As a result of the hydrolysis of methyl- and ethyltriethoxysilanes in alcohol it was possible to isolate polymethylsiloxanes with a complex tri- and tetracyclic structure in the amount of several percent from the hydrolyzates [1]. In all these substances the formation of rings is possible owing to the ethoxy or hydroxyl end groups. The most interesting [1] are hexa(ethylsilisesquioxane) $[C_2H_5SiO_{1.5}]_6$, octa(ethylsilsesquioxane) $[C_2H_5SiO_{1.5}]_8$ and the analogous octa(methylsilisesquioxane) [2] which do not contain functional groups.

As a result of the catalytic rearrangement of the hydrolysis products of the corresponding organotrichlorosilanes [3] 1-9% of crystalline cubic octamers of methyl-, ethyl-, N-propyl-, N-butyl and cyclohexylsilisesquioxanes were obtained and cubic silisesquioxane $[Cl_5C_6SiO_{1.5}]_8$ was found [4] in the hydrolysis products of pentachlorophenyltrichlorosilane. Andrianov and Zhdanov [5] put forward the suggestion that internal rings are formed as a result of the hydrolysis of phenyltrichlorosilane.

Cyclic compounds with a "urotropine" structure, where N is replaced by Si, and $CH_2$ by O were obtained from the hydrolysis products of $RSiCl_3$ (where R = tertiary $C_4H_9$, iso-$C_3H_7$) [6].

These data indicate that the hydrolysis of trifunctional monomers is accompanied by the formation of complex ring-shaped structures from which small amounts of the individual substances can be isolated. The main mass of the hydrolyzate does not lend itself to structural analysis, however, because it is an infusible and insoluble gel or powder. It may be assumed, however, that this mass, which is without functional groups, consists mainly of cyclosiloxanes combined in various ways.

We made an attempt to obtain some understanding of the structure of the hydrolysis products of alkyltrichlorosilane by the method of thermooxidative destruction. As was previously shown [7], at temperatures of the order of 200-400° atmospheric oxygen attacks the carbon atom near the silicon in the polymer molecule. As a result, hydroperoxides are first formed; these rapidly break down with the formation of formaldehyde and an OH radical. The OH radical then reacts with the silicon atom giving hydroxy compounds; the condensation of the latter, accompanied by the splitting off of water, leads to the formation of new siloxane bonds in the molecule.

For the thermooxidative destruction the previously synthesized methylchlorocyclosiloxanes [8] of the $[CH_3Si(Cl)O]_{4-7}$ series and ethylchlorocyclosiloxanes of the $[C_2H_5Si(Cl)O]_{3-5}$ series [9] were completely hydrolyzed with the formation of cyclic-stereometric polymers $[RSiO_{1.5}]_n$ with different, but specific, numbers of rings.
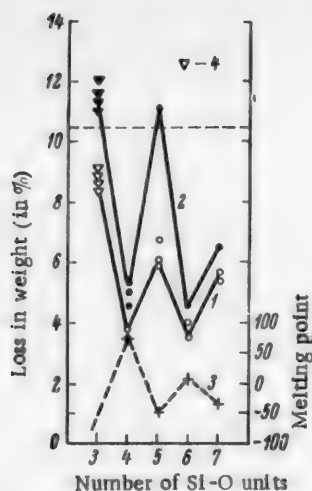
Fig. 1. Thermooxidative destruction of polymethylsiloxanes. 1) 350°, 2 hrs; 2) 400°, 2 hrs; 3) m. p. of methylchlorocyclosiloxanes; 4) data for the polymer from $CH_3SiCl_3$.
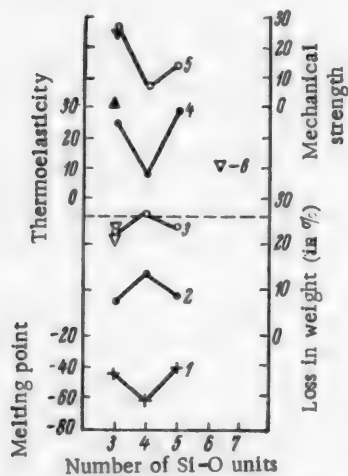


Fig. 2. Thermooxidative destruction of polyethylsiloxanes. 1) M. p. of ethylchlorocyclosiloxanes; 2) 220°, 22 hrs; 3) 300°, 1 hr; 4) thermoelasticity at 150°; 5) mechanical strength after 30 min at 200°; 6) data for the polymer from $C_2H_5SiCl_3$.

Polymers of methyl- and ethyltrichlorosilane were obtained in a similar manner. Figures 1 and 2 give the results of the thermooxidative destruction of these polymers expressed as the loss in weight relative to the number of Si—O units in the ring. The destruction was carried out for 2 hrs at 350 and 400° for polymethylsiloxanes and for 22 hrs (200°) and 1 hr (300°) for polyethylsiloxanes.

The data in Fig. 1 show the clear relationship between the degree of destruction and the number of Si—O units in the polymers; polymethylsiloxanes with an even number of units are destroyed more slowly than similar substances with an odd number of units. This phenomenon is observed at 350°, when the destructive decomposition of the radicals is still not complete, and at 400°, when this decomposition reaches a maximum (the dotted curve in Fig. 1 signifies the theoretical loss in weight corresponding to the disruption of all the radicals). The values of the weight loss for the polymer from methyltrichlorosilane justify the assumption that this polymer is composed of three-unit rings connected by siloxane bonds.

As a check, an analysis was made of the polymers after destruction at 400° (see Table).

Analysis of Polymethylsiloxanes After Thermooxidative Destruction

| Polymer | Found | | |
|---|---|---|---|
| | H (%) | C (%) | H/C |
| $[CH_3SiO_{1.5}]_n$ | 1.48 | 5.61 | 3.17 |
| $[CH_3SiO_{1.5}]_{4n}$ | 3.34 | 13.35 | 2.98 |
| $[CH_3SiO_{1.5}]_{5n}$ | 1.47 | 5.36 | 3.30 |
| $[CH_3SiO_{1.5}]_{6n}$ | 4.46 | 17.86 | 2.99 |
| $[CH_3SiO_{1.5}]_{7n}$ | 4.10 | 16.10 | 3.05 |

Note. Calculated for $CH_3SiO_{1.5}$ %: C 17.9; H 4.48.

The analytical data confirm the fact that maximum destruction occurs with polymers with an odd number of Si—O units. The greater than theoretical weight loss for these polymers with the retention of a certain number of methyl groups is evidently explained by the splitting off of a small amount of volatile products. As we found [7], complete detachment of the radicals does not take place even after heating at 450° for 24 hrs.

From a comparison of Figs. 1 and 3 it is seen that polymethylsiloxanes with an even number of Si—O units undergo the least destruction, i. e., that there is an inverse relationship with the melting points of the corresponding monomers.

In contrast to polymethylsiloxanes, in the case of polyethylsiloxanes (Fig. 2) it was found that polymers with an odd number of Si—O units undergo minimum thermooxidative destruction. In this instance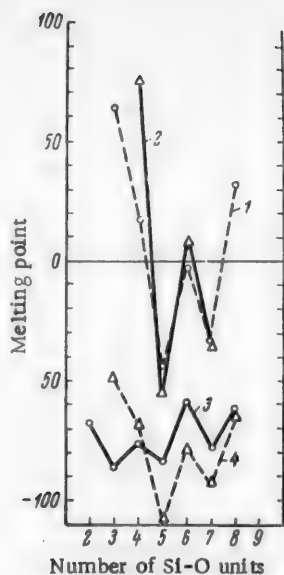, however, the inverse relationship with the melting points of the monomer is retained because in the case of diethylcyclosiloxanes the "even" polymers have lower melting points than the "odd" ones [13, 14]. The same relationship obtains for ethylchlorocyclosiloxanes (Fig. 2) [9] and, according to our data, for ethylcyclosiloxanes also: triethylcyclotrisiloxane has m. p. of 100°, tetraethylcyclotetrasiloxane, m. p. of 107° and pentaethylcyclopentasiloxane, m. p. of 82°.

Fig. 3. Melting points. 1) Dimethyl-
cyclosiloxanes [10]; 2) methylchloro-
cyclosiloxanes [8]; 3) dimethylsiloxanes
[12]; 4) methylcylcosiloxanes [8, 11].

The values of the weight losses for the hydrolysis products of ethyltrichlorosilane justify the assumption that this polymer consists mainly of three-unit rings connected by siloxane bonds.

A consideration of the experimental data leads to the conclusion that in this instance a relationship exists between the melting points of the initial monomers and the properties of the corresponding polymers. The "even number factor" (to use the term proposed by V. V. Korshak) embraces a wide range of substances including both those with open chains (e. g., carboxylic acids) and cyclic hydrocarbons (e. g., cycloparaffins). The influence of the even number factor was also established for high-molecular compounds. Korshak and his co-workers [15, 16] found a marked difference in the melting points of polyesters of even-membered and odd-membered dicarboxylic acids: all the polyesters of even-membered dicarboxylic acids melt at higher temperatures, like the "even" acids themselves. The same relationship was established for polyurethanes and polyamides. It is very interesting that carboxylic acids with an even number of carbon atoms have a higher decarboxylation temperature [17].

The presence of the even-number factor is explained by the influence of polar forces between the molecules; with an increase in these forces the packing density of the polymers increases [15, 18] and the polymer must be less subject to thermooxidative reduction, as is seen in the case of polyalkylsiloxanes.

An increase in the packing density must also lead to an increase in the mechanical strength and the thermoelasticity of films of the polymer; this is confirmed by the data of Fig. 2 (curves 4 and 5).

X-rays *    showed that the polymer obtained by the hydrolysis of $SiCl_4$ is completely amorphous. Polymethylsiloxane $(CH_3SiO_{1.5})_4n$ was found to be amorphous-crystalline. The simultaneous presence of a fine-crystalline and amorphous structure is still more clearly expressed in the case of the polymer $(CH_3SiO_{1.5})_4n$. The structure of polyalkylsiloxanes is undoubtedly very complex and is far from showing complete regularity. The conclusion may nevertheless be drawn that a certain number of cyclic trimers exists in the hydrolysis products of $CH_3SiCl_3$ and $C_2H_4SiCl_3$.

## EXPERIMENTAL

Samples of polyalkylsiloxanes were prepared by the hydrolysis of the corresponding monomers dissolved in one volume of toluene. After the samples had been washed free from HCl they were dried for 4 hrs at 120° and crushed. To determine the weight loss as a result of thermooxidative destruction ~ 0.2 g weighed samples of the polymers in open crucibles were placed in a muffle furnace at the given temperature. The hydrolysis and destruction experiments were repeated and gave reproducible results. The intial alkylchlorocyclosiloxanes corresponded to the characteristics found previously [8, 9].

The determination of the thermoelasticity and mechanical strength of the polyethylsiloxanes (directly after hydrolysis they were soluble in toluene) was carried out with lacquer films, 50 μ thick, applied to copper foil, 0.1 mm thick.

The time required for cracks to appear in the film when it was wound around a 3 mm diameter rod served as the criterion of thermoelasticity. The mechanical strength was characterized as the number of reciprocal movements of a 250 g ball along the film in a reversing apparatus up to the moment of perforation of the film as a result of the stress applied to the ball and the copper plate.

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*   Taken at our request by K. V. Krylov.

SUMMARY

1. The method of thermooxidative destruction was proposed for the investigation of the structure of poly-alkylsiloxanes.

2. It was found that the degree of destruction of the hydrolysis products of methylchlorocyclosiloxanes and ethylchlorocyclosiloxanes is characterized by the even number factor in relation to the number of Si−O units in the initial rings. The hydrolysis products of methyl- and ethyltrichlorosilane are evidently complex structures of cyclic trimers.

3. The hypothesis was advanced that the even number factor and the capacity for destruction of polyalkyl-siloxanes depend on the packing density.

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* Original Russian pagination. See C. B. translation.

# THE SYNTHESIS OF o-CARBOXY- AND
# o-CARBOXYDIMETHOXYBENZALBARBITURIC ACIDS*

### E. I. Chukhina

The main task of the present work was the study of the synthesis of o-carboxy- and o-carboxydimethoxybenzalbarbituric acid containing two acid radicals in the molecule, i. e., o-aldehydebenzoic and opianic acids; these compounds have not been previously described in literature.

o-Carboxybenzalbarbituric acid was synthesized in two ways: a) by the general method of preparing C-substituted barbituric acid from urea and o-carboxybenzylidenemalonic ester [2]; b) by the condensation of o-aldehydebenzoic acid with barbituric acid in an aqueous medium.
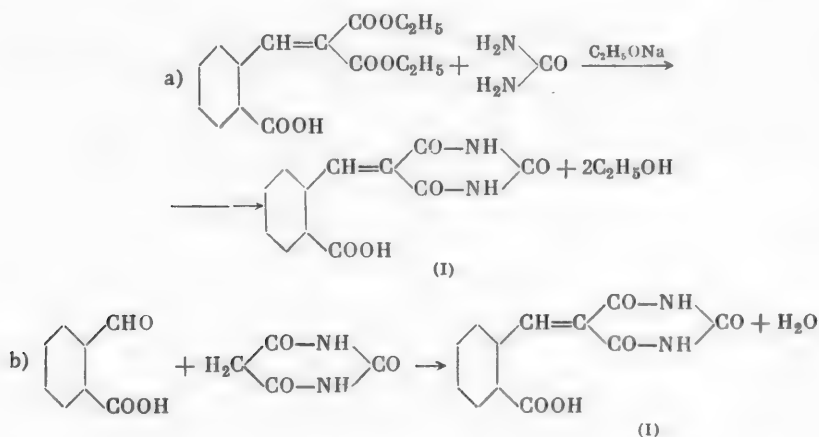


o-Carboxybenzalbarbituric acid is a solid crystalline substance with a m. p. of 276-278°. The structure of the compound obtained was established 1) by oxidation, which led to the formation of alloxan and 2) by reduction, as a result of which o-carboxybenzylbarbituric acid (II) was evidently obtained. As a result of the alkaline hydrolysis of this compound o-carboxybenzylmalonic acid (III) was isolated; this compound was first obtained by Wislicenus from phthalylmalonic ester [3] which after being heated is converted to o-carboxyhydrocinnamic acid (IV).(see diagrams at top of next page).

When o-carboxybenzalbarbituric acid was synthesized by the first method (from urea and o-carboxybenzylidenemalonic ester) by-products of the reaction were also obtained: 1) o-carboxycinnamic acid, 2) a crystalline substance of unestablished structure, and 3) a substance with a high nitrogen content which, according to the nitrogen analysis and the value of the gram-equivalent was the diureide of o-carboxybenzylidenemalonic ester (V). (see diagram on following page).

Since a comparatively low yield (45-50%) of the main product was obtained in this reaction the condensation of o-aldehydebenzoic acid with barbituric acid in an aqueous medium was investigated. A similar conden-

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* The present work is the continuation of that commenced together with V. M. Rodionov [1].
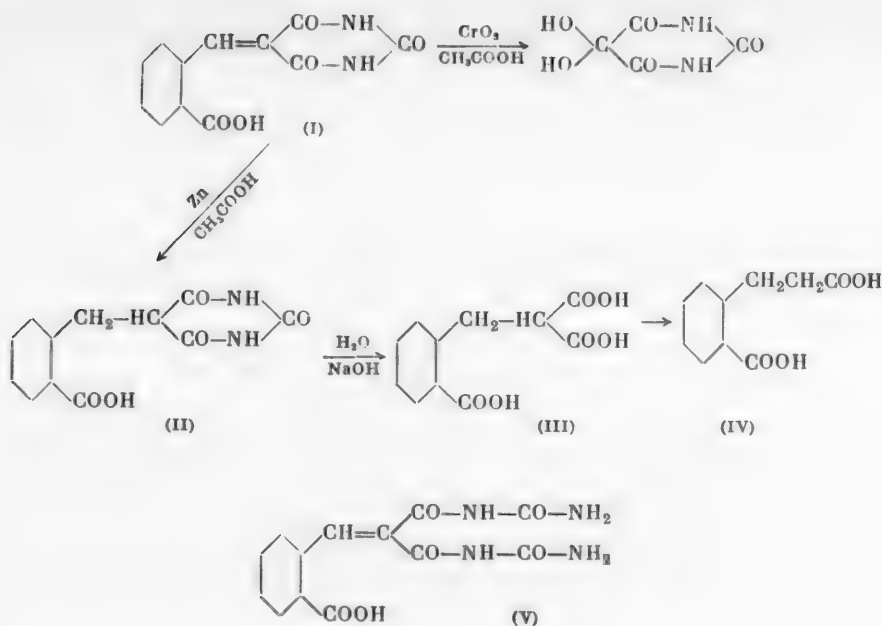
Scheme I → (CrO₃/CH₃COOH) and (Zn/CH₃COOH):

$(I)$ o-carboxybenzalbarbituric structure $\xrightarrow[CH_3COOH]{CrO_3}$ hydroxy derivative

$(I) \xrightarrow[CH_3COOH]{Zn} (II)$

$(II) \xrightarrow[NaOH]{H_2O} (III) \rightarrow (IV)$

$(V)$ structure with CH=C(CO–NH–CO–NH₂)(CO–NH–CO–NH₂), COOH

By this method, o-carboxybenzalbarbituric acid, which is difficultly soluble in water, was obtained with a good yield and without the formation of reaction by-products.

The condensation of barbituric acid with opianic acid was carried out under the same conditions; as a result a 75-85% yield of o-carboxydimethoxybenzalbarbituric acid (VI), which is also difficultly soluble in water, was obtained.

Scheme: (CHO, H₃CO, H₃CO, COOH) + H₂C(CO–NH)(CO–NH)CO → o-carboxydimethoxybenzalbarbituric acid (VI)
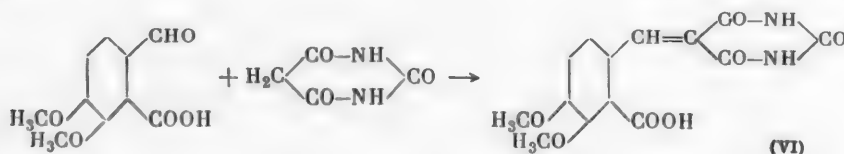
The synthesis of these two benzal derivatives of barbituric acid with a good yield via the sodium salts of o-aldehyde acids was also found to be possible.

Considerable difficulties were encountered in the determination of the gram-equivalents of the barbituric acid derivatives obtained. The combustion of the Na salts of o-carboxy- and o-carbethoxydimethoxybenzalbarbituric acids in the presence of $HNO_3$ and $H_2SO_4$ [5] made it possible to determine the quantitative Na content fairly accurately and to calculate the gram-equivalent of the acid from this.

## EXPERIMENTAL

The condensation of o-carboxybenzylidenemalonic ester from urea in the presence of sodium ethylate. When 25 g of o-carboxybenzylidenemalonic ester and 10 g of urea were heated in 40 ml of an alcoholic solution of sodium ethylate (from 4 g of Na) and the mixture was acidified with HCl (1 : 1), 3 solid fractions were obtained by fractional precipitation*:

* The precipitates were first treated with ether; o-carboxycinnamic acid was found in the ethereal solutions.

1) 1.96 g of a substance of unidentified structure, in the form of colorless needles with a m. p. of 239-240° (from alcohol);

2) 10.55 g of o-carboxybenzalbarbituric acid in the form of colorless crystals with a m. p. of 276-278°* (from water, with decomp.).

Found %: C 55.60, 55.37; H 2.91, 3.00; N 10.79, 10.82; M 253, 257. $C_{12}H_8O_5N_2$. Calculated %: C 55.39; H 3.08; N 10.88. M 260.**

3) 0.15 g of the diureide of o-carboxybenzylidenemalonic ester in the form of colorless needles (from water) which did not melt up to a temperature of 310-315° and above and was soluble in an aqueous solution of soda.

Found %: N 17.31, 17.43. M 318, 316. $C_{13}H_{12}O_6N_4$. Calculated %: N 17.50. M 320.

When o-carboxybenzalbarbituric acid was oxidized with $CrO_3$ in glacial acetic acid [2],alloxan was formed. When 0.5 g of o-carboxybenzalbarbituric acid was reduced with zinc dust in $CH_3COOH$ 0.31 g of o-carboxybenzylbarbituric acid was precipitated in the form of colorless needles with a m. p. 236-237°*** (from water).

Found %: N 10.71, 10.80. $C_{12}H_{10}O_5N_2$. Calculated %: N 10.69.

After the alkaline hydrolysis of 0.25 g of o-carboxybenzylbarbituric acid 0.15 g of o-carboxybenzylmalonic acid was obtained in the form of colorless needles with a m. p. of 170-174° (from water; with decomp.).

Found %: C 55.31; H 4.51. $C_{11}H_{10}O_6$. Calculated %: C 55.46; H 4.20.

The o-carboxyhydrocinnamic acid formed by the decarboxylation of the hydrolysis product when heated to 190° showed no depression of the melting point in a mixed melt with o-carboxyhydrocinnamic acid, specially obtained.****

The condensation of o-aldehydebenzoic and opianic acids with barbituric acid in water. Equimolecular amounts of barbituric acid and the aldehydic acid were dissolved in water (0.8 molar solution) by heating in a flask, equipped with a stirrer, on a boiling water bath; o-aldehydebenzoic acid was then added to the solution in small quantities. After the solution had been heated for 3 hrs a precipitate of o-carboxybenzalbarbituric acid was soon precipitated; this was purified by dissolving in a solution of soda and was recrystallized from water after it had been precipitated from the acidified soda solution. 7.00 g of o-carboxybenzalbarbituric acid was obtained from 5.00 g of o-aldehydebenzoic acid and 4.27 g of barbituric acid. 3.60 g of o-carboxydimethoxybenzalbarbituric acid was obtained in the form of colorless crystals with a m. p. of 258-259° (from water; with decomp.) from 2.00 g of opianic acid and 2.19 g of barbituric acid.

Found %: C 52.38, 52.45; H 3.70, 3.80; N 8.56, 8.60. M 319. $C_{14}H_{12}O_7N_2$. Calculated %: C 52.50; H 3.75; N 8.75. M 320.

The condensation of the Na salts of both the o-aldehydic acids with barbituric acid took place under conditions similar to those for the condensation of the acids themselves. The condensation products remained in the aqueous solution and were precipitated on acidification. 8.80 g of o-carboxydimethoxybenzalbarbituric acid was formed from 6.00 g of the Na salt of opianic acid. This acid contains 1 mole of water of crystallization.

Found %: $H_2O$ 5.28. $C_{14}H_{12}O_7N_2 \cdot H_2O$. Calculated %: $H_2O$ 5.32.

The percentage Na content in the samples of the Na salts of both acids which were prepared was determined by the combustion of the substance in the crucible in the presence of $H_2SO_4$ and $HNO_3$ [5] and the gram-equivalent of the acid was calculated from it.

The salts of both derivatives of barbituric acid contain 1 mole of water of crystallization.

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* To determine the melting point the capillary containing the substance was lowered into an apparatus heated to 237°.

** The substance was first dried at 110-120°.

*** The capillary containing the substance was lowered into an apparatus heated to 229°.

**** o-Carboxycinnamic acid was prepared by Titley's method [6] and was reduced to o-carboxyhydrocinnamic acid.

Found %: $H_2O$ 5.79. $C_{12}H_7O_5N_2Na \cdot H_2O$. Calculated %: $H_2O$ 6.00.

Found %: Na 7.89; g-equiv. 269. $C_{12}H_7O_5N_2Na$.[*] Calculated %: Na 8.15; g-equiv. 260.

Found %: Na 6.70; g-equiv. 321. $C_{14}H_{11}O_7N_2Na$. Calculated %: Na 6.73; g-equiv. 320.

## SUMMARY

1. It was shown that as a result of the condensation of o-carboxybenzylidenemalonic ester with urea in the presence of sodium alcoholate the main product obtained is o-carboxybenzalbarbituric acid with a yield of 45-50%, calculated on the initial ester. The structure of this compound was established.

2. A simpler method of synthesizing o-carboxy- and o-carboxydimethoxybenzalbarbituric acids by the condensation of o-aldehydic acids or their Na salts with barbituric acid in an aqueous medium with a 75-85% yield was found.

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[*] The Na content was determined in the dehydrated salts.

[**] Original Russian pagination. See C. B. translation.

# THE SYNTHESIS OF SUBSTANCES WITH A HYPOTENSIVE ACTION — DERIVATIVES OF QUATERNARY AMMONIUM BASES

## IV. QUATERNARY SALTS OF β-PHENYLISOPROPYLDIMETHYLAMINE

### I. B. Simon

It is known that the conversion of the secondary amino group of N-alkylphenylethylamine into a tertiary group and, in particular, the transition to a quaternary ammonium salt modifies the physiological properties of the amine which acts as a depressant instead of a stimulant [1]. For example, according to the data of Alles [2] phenylethyltrimethylammonium hydroxide has a hypotensive action. N-Alkyl derivatives of other analogs of phenylethylamine such as, for example, β-(o-anisyl)-propylmethylamine, or "orthoxin" [3], β-(o-anisyl)-isopropyldimethylamine [3], etc. have a powerful depressant action. It was, therefore, of interest to determine the nature of the influence on the physiological activity of the conversion of the primary amino group in another analog of phenylethylamine — β-phenylisopropylamine (phenamine) — to the corresponding quaternary salts.

For this purpose the quaternary ammonium salts of "phenamine" were synthesized by the treatment of β-phenylisopropyldimethylamine by various alkyl halides.

The Properties of Quaternary Ammonium Salts of β-Phenylisopropylamine
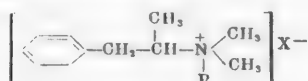


| R | X | Molec. wt. of radical | Empirical formula | Melting point | Results of nitrogen analysis * (%) | | Depressant activity | Remarks |
|---|---|---|---|---|---|---|---|---|
| | | | | | found | calc. | | |
| H | Cl | 1 | $C_{11}H_{18}NCl$ | 157—158° | — | — | · · | White crystals |
| $CH_3$ | I | 15 | $C_{12}H_{20}NI$ | 228—230 | 4.56, 4.21 | 4.57 | -\|- | |
| $C_2H_5$ | I | 29 | $C_{13}H_{22}NI$ | 151 | 4.08, 5.95 | 4.38 | + | Yellowish crystals |
| n-$C_3H_7$ | I | 43 | $C_{14}H_{24}NI$ | 188—189 | 4.26, 4.29 | 4.20 | + | |
| iso-$C_3H_7$ | I | 43 | $C_{14}H_{24}NI$ | 165 | 4.11, 4.35 | 4.20 | -\| | |
| n-$C_4H_9$ | I | 57 | $C_{15}H_{26}NI$ | 113—114 | 4.02, 3.96 | 4.04 | -\|- | White hygroscopic crystals |
| iso-$C_4H_9$ | I | 57 | $C_{15}H_{26}NI$ | 108—110 | 3.92, 3.74 | 4.04 | + | |
| iso-$C_5H_{11}$ | I | 71 | $C_{16}H_{28}NI$ | 100—102 | 3.20, 3.26 | 3.88 | +-+ | |
| $C_6H_{11}$ | I | 83 | $C_{17}H_{28}NI$ | 124 | 3.80, 3.92 | 3.76 | ++ | White crystals |
| n.-$C_6H_{13}$ | I | 85 | $C_{17}H_{30}NI$ | 77—78 | 3.89, 3.82 | 3.73 | ++ | Yellow, very hygroscopic crystals |
| $C_6H_5CH_2$ | Cl | 91 | $C_{18}H_{24}NCl$ | 185—187 | 4.81, 4.35 | 4.84 | +-+-\| | White crystals |

* The analyses were carried out in the microanalysis laboratory of our Institute.

A list of the quaternary ammonium salts of β-phenylisopropylamine obtained and their properties is given in the table. A comparative investigation of the hypotensive properties of the quaternary ammonium salts of β-phenylisopropylamine was carried out in the School of Pharmacology of the Kharkov Medical Institute (M. S. Kharchenko) in acute experiments on rabbits and cats. From the table it is seen that all the quaternary ammonium salts of β-phenylisopropylamine have a depressant effect which increases with increasing molecular weight of the radical.

## EXPERIMENTAL

β-Phenylisopropyldimethylamine.  230 g (5 moles) of 90% formic acid was added with cooling and stirring to 135 g (1 mole) of β-phenylisopropylamine and 200 ml (2.2 mole) of 35% formalin was then added gradually. The mixture was heated on a water bath for 18 hrs and when it had cooled 100 ml of concentrated hydrochloric acid was added.  The excess formic acid and formaldehyde were distilled until $^{1}/_{4}$ of the contents were left in the distillation flask.  The residue was transferred to a separating funnel and 200 ml of 10% caustic soda was added with cooling;  the mixture was then extracted several times with ether.  The ethereal extract was dried over alkali and distilled.  The residue was distilled under vacuum;  the b. p. was 115-118° (20 mm).  The yield was 120 g (70%).  The m. p. of the hydrochloride was 157-158°.  According to Woodroof's data [3], β-phenylisopropyldimethylamine has a b. p. of 100° (12 mm), its hydrochloride has a m. p. of 159-161°.

The quaternary salts of β-phenylisopropyldimethylamine.  Equimolecular amounts of β-phenylisopropyldimethylamine and the corresponding alkyl halide, dissolved in a small amount of dry benzene, were placed in a small flask, equipped with a reflux condenser.  The mixture was heated on a water bath for 3 hrs.  The benzene was distilled and the precipitate formed was recrystallized from anhydrous alcohol or dry acetone.  The yield of the salts was 60-85%.  They were all readily soluble in water, alcohol and acetone and difficultly soluble in ether, benzene, xylene and petroleum ether.  The aqueous solutions had a neutral reaction to litmus and were stable at 100°.

## SUMMARY

1. β-Phenyl isopropyltrimethylammonium iodide, β-phenylisopropyldimethylethylammonium iodide, β-phenylisopropyldimethylpropylammonium iodide, β-phenylisopropyldimethylbutylammonium iodide, β-phenylisopropyldimethylisobutylammonium iodide, β-phenylisopropyldimethylisoamylammonium iodide, β-phenylisopropyldimethylcyclohexylammonium iodide, β-phenylisopropyldimethylhexylammonium iodide, β-phenyl-, isopropyldimethylbenzylammonium chloride and β-phenylisopropyldimethylisopropylammonium iodide were obtained by treating β-phenylisopropyldimethylamine with alkyl halides.

2. All the quaternary salts obtained have a depressant effect which increases with increasing molecular weight of the radical.

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# THE REACTIVITY OF α,β-UNSATURATED KETONES AND β-KETONE HALIDES IN THE KIZHNER REACTION

A. P. Meshcheriakov, L. V. Petrova, and Iu. P. Egorov

According to N. M. Kizhner [1, 2], α,β-unsaturated ketones of the type R—C—C=C—C and
$$\underset{\overset{||}{O}}{R-C}-\underset{C}{C}=C-C$$
and

R—C—CH=C—C—C give pyrazoline bases with hydrazine which decompose during slow distillation only in
the presence of a mixture of catalysts (Pt and KOH), liberating nitrogen and forming the corresponding cyclopropane hydrocarbon. It is not necessary, however, to observe this condition in all instances where the pyrazoline base is concerned. For example, in order to obtain cyclopropane hydrocarbons the decomposition of pyrazoline bases was later [3] carried out in the presence of KOH only. The formation of a cyclopropane hydrocarbon as a result of the decomposition of a pyrazoline base during heating can, however, take place in the complete absence of catalysts (both Pt and KOH) at an appropriate temperature, which is somewhat higher than the boiling point of the pyrazoline base.

According to Kizhner [4], the decomposition of the alkylidene hydrazine under the influence of catalytic amounts of KOH precedes its isomerization to the unstable tautomeric form which decomposes with the liberation of nitrogen in a similar manner to aromatic diazo compounds.

In our opinion the decomposition of the pyrazoline bases can evidently take place via a stage in which a biradical is formed, the latter then giving rise to the cyclopropane hydrocarbon.
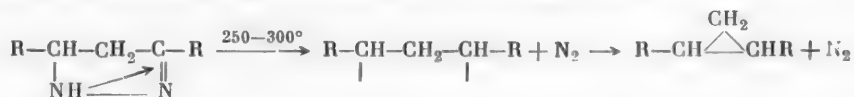


From the mixture of ketones: 4,6,6-trimethyl-3-hepten-2-one and 4,4-dimethyl-3-isopropylidene-2-pentanone we obtained for the first time a mixture of 3,5-dimethyl-5-neopentyl- and 3,5,5-trimethyl-4-tert-butylpyrazolines which on distillation at atmospheric pressure without a catalyst gave a mixture of two isomers: 1,3-dimethyl-3-neopentylcyclopropane and 1,2,2-trimethyl-3-tert-butylcyclopropane. When distilled in the presence of catalysts (Pt and KOH) these pyrazoline bases form a different mixture: 4,6,6-trimethyl-3-heptene and 1,2,2-trimethyl-3-tert-butylcyclopropane (with a predominance of the alkene).

We explain the presence of an alkene in this mixture by the fact that under the influence of KOH and Pt at high temperature the trimethylene ring of 1,3-dimethyl-3-neopentylcyclopropane is broken and 4,6,6-trimethyl-3-heptene is formed.
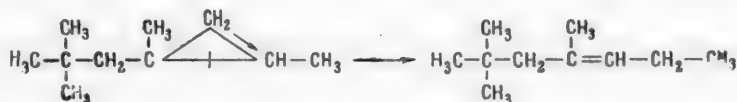
In addition to $\alpha,\beta$-unsaturated ketones, $\beta$-chloroketones, obtained by the reaction of acid chlorides with alkenes, may be used successfully for obtaining pyrazoline bases [5-7]. When reacted with an alcoholic solution of hydrazine the 2-chloro-2-methyl-4-pentanone and 2-chloro-2-methyl-4-undecanone, which we synthesized by the catalytic method, gave 5,5-dimethyl-3-pentylpyrazoline and 5,5-dimethyl-3-heptylpyrazoline. The reaction takes place according to the following system:



$$R = n\text{-}C_5H_{11}, \ n\text{-}C_7H_{15}$$
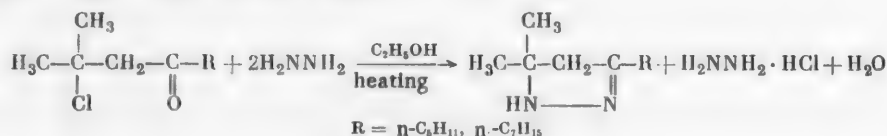
On slow distillation in the presence of Pt or KOH the above-mentioned pyrazoline bases gave 1,1-dimethyl-N-amylcyclopropane and 1,1-dimethyl-N-heptylcyclopropane. When these pyrazoline bases were heated to constant boiling at atmospheric pressure in the presence of a catalyst the same hydrocarbons were formed.

Since the pyrazoline bases which we investigated have relatively high boiling points (the boiling points of these compounds at atmospheric pressure are above 200°) at which they already decompose into nitrogen and a cyclopropane hydrocarbon, it was suggested that the low-boiling pyrazoline would also decompose without a catalyst (Pt and KOH) at increased temperature, with the formation of cyclopropane hydrocarbons.

We carried out experiments on the thermal decomposition of 3,5,5-trimethylpyrazoline at 420-440°. The data of the gas analysis indicated that when the base decomposes,1 molecule of nitrogen is liberated from 1 molecule of the latter and 3 molecules of methane are formed; in addition, a mixture of alkenes, in which tetramethylethylene predominates, is formed. On the basis of these data it may be assumed that the decomposition of the pyrazoline base takes place according to the following system:
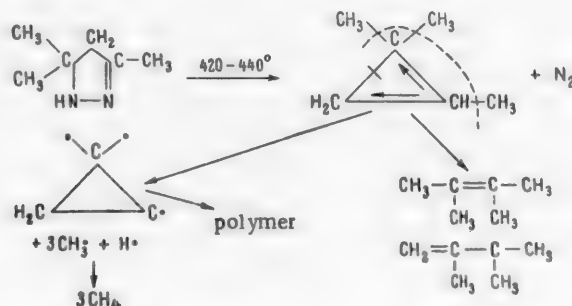


As may be seen from the system, the 1,1,2-trimethylcyclopropane formed under high-temperature conditions is mainly demethylated and gives methane while in the molecules of the cyclopropane hydrocarbon (of which a small amount remains) the ring is is broken and a mixture of alkenes with a predominance of tetramethylethylene is formed.

In addition to chemical methods we used the combined dispersion spectrum method for proving the structure of the cyclopropane hydrocarbons obtained.

The combined dispersion spectra of cyclopropane compounds are still insufficiently studied [8-11]. In the combined dispersion spectra of trimethylene compounds several characteristic frequencies were, however, established [12], from which it was possible to judge the presence of a three-membered ring in these compounds. Among the frequencies of this type there are frequencies in the 3000-3100 cm$^{-1}$ region which correspond to the vibrations of the C−H bond of the ring.

Cyclopropane and its mono-substituted derivatives have frequencies of 1190 and 870 cm$^{-1}$ which correspond to the antisymmetrical and symmetrical vibrations of the ring, respectively. There are 3-4 frequencies instead of the two above-mentioned frequencies (1190 and 870 cm$^{-1}$) in the spectra of disubstituted cyclopropanes.

Only two spectra of cyclopropane compounds with a quaternary carbon atom are given in the literature, i. e., 1,1-dimethylcyclopropane and 1,1,2-trimethylcyclopropane [9, 10]. In the spectra of these compounds there are also lines in the above-mentioned regions, indicating the presence of a three-membered ring. In addition, there is also a fairly intense line with a frequency of $\sim 678$ cm$^{-1}$. This frequency is evidently characteristic for a gem-substituted carbon atom in the ring (average frequency 706 cm$^{-1}$ in the spectrum of 1,1-dimethylcyclohexane [10]).

## EXPERIMENTAL

The preparation and decomposition of 3,5-dimethyl-5-neopentyl- and 3,5,5-trimethyl-4-tert -butylpyrazolines. A mixture of ketones was used to obtain the given pyrazolines: 4,6,6-trimethyl-3-penten-2-one and 4,4-dimethyl-3-isopropylidene-2-pentanone, synthesized from Butlerov's diisobutylene ( 80% 2,2,4-trimethyl-4-pentene and 20% 2,2,4-trimethyl-3-pentene) by Kondakov's method [5]. The first isomer is predominant in this mixture of ketones.

B. p. 65-68° (1-2 mm), $d_4^{20}$ 0.8419, $n^{20}$D 1.4467, MR$_D$ 48.079; calc. 47.927. Found %: C 77.35; H 11.57. $C_{10}H_{18}O$. Calculated %: C 77.71; H 11.70.

The 2,4-dinitrophenylhydrazone with a m. p. of 159-160° (from ethyl alcohol) was obtained.

Found %: N 16.77. $C_{16}H_{22}O_4N_4$. Calculated %: N 16.76.

The pyrazoline base was obtained by boiling an alcoholic solution of the hydrazine hydrate for 6 hrs with an alcoholic solution of the mixture of ketones obtained. 41.0 g (72.2%) of pyrazoline base was obtained from 61 g of the mixture of ketones and 41 g of hydrazine hydrate. Taking the structure of the initial ketones into consideration it must be assumed that the base is a mixture of 3,5-dimethyl-5-neopentyl- and 3,5,5-trimethyl-4-tert -butylpyrazolines with a predominance of the first isomer.

The base was decomposed in a small copper flask, equipped with a fir-tree shaped fractionating column, connected to a horizontal condenser. 8-10 g of KOH, a catalytic quantity of 5% platinum on charcoal and 48 g of the mixture of isomeric pyrazolines were placed in the flask. The decomposition products were distilled at 128-139°. The hydrocarbons were separated from the undecomposed base in a column (with an efficiency of 18 theoretical plates), washed free from traces of base with 50% CH$_3$COOH, then washed with a 25% NaOH solution and water, dried with CaCl$_2$ and distilled twice over Na in a column. 24 g (50%) of a mixture of hydrocarbons was obtained.

B. p. 144-145°, $d_4^{20}$ 0.7496, $n^{20}$D 1.4243, MR$_D$ 47.48; calc. 46.18. The exaltation of 1.3 characterizes the presence of one double bond.

On the basis of an analysis of the combined dispersion spectrum of the mixture of hydrocarbons the presence of a double bond (1663 cm$^{-1}$) and a small amount of a hydrocarbon with a three-membered ring was established.

The product of the catalytic decomposition of pyrazolines, therefore, consists mainly of an alkene and a small amount of a hydrocarbon with a trimethylene ring.

The structure of the alkene obtained (2,2,4-trimethyl-4-heptene) was established by oxidizing it with a 1% solution of KMnO$_4$. The following oxidation products were isolated.

a) Methyl neopentyl ketone with a b. p. of 126-130°. Its semicarbazone with a m. p. of 123-125° was obtained; literature data: m. p. 124° [13].

Found %: N 24.83. $C_8H_{17}ON_3$. Calculated %: N 24.56.

b) Propionic acid with a b. p. of 141-145°. It was identified from its acid equivalent by titrating with 0.1 N NaOH.

Found: equiv. 520. $C_3H_6O_2$. Calculated: equiv. 540.

By repeated distillation of the low-boiling fractions of the oxidation products containing ketone it was possible to isolate a cyclopropane hydrocarbon.

B. p. 144-145°, $d_4^{20}$ 0.7575, $n^{20}$D 1.4250, MR$_D$ 47.04; calc. 46.18. Exaltation 0.8 due to a three-membered ring. Found %: C 85.68; H 14.33. $C_{10}H_{20}$. Calculated %: C 85.63; H 14.37.

Combined dispersion spectrum,* $\Delta\gamma$ cm$^{-1}$:  220 (9), 320 (9), 463 (9), 636 (0), 702 (2), 720 (1), 767 (1), 799 (1), 1109 (2), 1200 (0), 1409 (1), 1447 (1), 2868 (1), 2910 (5), 2921 (1), 2964 (1), 2995 (1).

After the removal of the alkene (by oxidation with a 1% solution of KMnO$_4$) we were, therefore, left with only 1,2,2-trimethyl-3-tert -butylcyclopropane.

In another experiment a mixture of 3,5-dimethyl-5-neopentyl- and 3,5,5-trimethyl-4-tert -butylpyrazolines was distilled at atmospheric pressure. The distillation temperature of the hydrocarbons was 120-140°. A hydrocarbon was isolated with a yield of 10% after the mixture had been distilled twice over Na.

B. p. 144-145°, $d_4^{20}$ 0.7559, $n^{20}$D 1.4213, MR$_D$ 46.94; calc. 46.18. The exaltation of 0.76 characterizes a three-membered ring.

Combined dispersion spectrum, $\Delta\gamma$ cm$^{-1}$:  528 (1 b), 688 (0), 714 (4), 748 (3 b), 775 (2 b), 825 (0), 853 (1), 884 (1), 910 (1), 933 (2), 980 (0), 1098 (3 b), 1162 (0), 1202 (2), 1245 (3 b), 1366 (1), 1392 (0), 1445 (4 b), 1461 (1), 1642 (0), 1662 (0), 2870 (5 b), 2902 (3 b), 2956 (8 b), 2988 (2).

In addition to the frequencies characteristic for a gem-substituted three-membered ring (714 and 2988 cm$^{-1}$) frequencies of the C=C bonds (1642 and 1662 cm$^{-1}$) were detected. The intensity of these lines denotes only a small admixture of alkenes.

We also carried out observations on the stability of a mixture of bases at room temperature in the presence of KOH, K$_2$CO$_3$, Al$_2$O$_3$ and Ba(OH)$_2$ over a period of 3 days. When allowed to stand in light these bases decompose appreciably in the presence of KOH and K$_2$CO$_3$ from the first moment of contact (liberation of nitrogen). In the presence of Al$_2$O$_3$ and Ba(OH)$_2$ the decomposition process is very sluggish.

The synthesis of 2-chloro-2-methyl-4-nonanone.   To obtain 1,1-dimethyl-2-pentylcyclopropane we synthesized 2-chloro-2-methyl-4-nonanone from capronyl chloride and isobutylene in the presence of 10% ZnCl$_2$. The capronyl chloride had the following properties: b. p. 65-70° (45-50 mm), $d_4^{20}$ 1.0416 (literature data: b. p. 150-153° [14]). The synthesis of 2-chloro-2-methyl-4-nonanone was carried out in a metal boat at room temperature with constant shaking on a rocker for 18 hrs. The isobutylene was added to the boat in liquid form. 238 g (97.5%) of crude 2-chloro-2-methyl-4-nonanone was obtained from 172 g of the acyl chloride and 120 g of isobutylene. Two fractions were obtained by distilling it under vacuum: 1st fraction, b. p. 78-90° (2 mm), $d_4^{20}$ 0.8896, $n^{20}$D 1.4480, 58 g; 2nd, b. p. 90-95° (2 mm), $d_4^{20}$ 0.8782, $n^{20}$D 1.4538, 62.5 g.

Since, as was repeatedly noted, HCl is split off during the process of distillation of the chloroketone, the 1st fraction, which consisted mainly of an unsaturated ketone with the composition C$_{10}$H$_{18}$O, contained 2-chloro-2-methyl-4-nonanone as an admixture. The 2nd fraction was mainly 2-chloro-2-methyl-4-nonane.

To obtain 2-methyl-2-nonen-4-one in the pure form the 1st fraction was treated with a saturated solution of K$_2$CO$_3$ by boiling on a water bath for 6 hrs. Since the ketone still contained traces of chlorine it was washed with a saturated solution of soda, then with water and was finally dried with CaCl$_2$. A 62.6% yield of 2-methyl-2-nonen-4-one was obtained by distillation.

B. p. 205-207°, $d_4^{20}$ 0.8524, $n^{20}$D 1.4522, MR$_D$ 48.57; calc. 47.92. Found %: C 76.90; H 11.61. C$_{10}$H$_{18}$O. Calculated %: C 77.90; H 11.68. (The discrepancy in the analysis evidently results from the residual traces of chlorine.)

The semicarbazone of 2-methyl-2-nonen-4-one with a m. p. of 79-80° (from 50% C$_2$H$_5$OH) was obtained.

Found %: N 21.12. C$_{11}$H$_{21}$ON$_3$. Calculated %: N 21.32.

The preparation of 3-pentyl-5,5-dimethylpyrazoline. 31 g of 2-chloro-2-methyl-4-nonanone and an alcoholic solution containing 8.2 g of hydrazine hydrate were taken for the reaction. When they were mixed heat was evolved and the temperature rose to 60-65°. The mixture was subsequently boiled with constant stirring for 6 hrs. After the alcohol and unreacted hydrazine hydrate had been distilled off the reaction product was dried with KOH and distilled. The yield of 3-pentyl-5,5-dimethylpyrazoline was 97.4%.

B. p. 215-220° (765 mm), $d_4^{20}$ 0.8797, $n^{20}$D 1.4580, MR$_D$ 51.57; calc. 51.35.

The catalytic decomposition of 3-pentyl-5,5-dimethylpyrazoline. As indicated above, the decomposition of the pyrazoline base (26.5) was carried out in the presence of 10 g of KOH and a catalytic quantity of 5% platinum

* The spectrum of this compound is incomplete.

on charcoal. The hydrocarbon was distilled at 128-170°, washed with 50% $CH_3COOH$ (to remove traces of base), neutralized with a 25% NaOH solution, washed with water and dried with $CaCl_2$. A 66.0% yield of 1,1-dimethyl-2-N-pentylcyclopropane was obtained by distilling the treated hydrocarbon twice over Na in a column with an efficiency of 18 theoretical plates.

B. p. 156.5-157° (740 mm), $d_4^{20}$ 0.7520, $n^{20}D$ 1.4205, $MR_D$ 47.06; calc. 46.18. Exaltation due to a three-membered ring 0.88. Found %: C 85.62; H 14.50. $C_{10}H_{20}$. Calculated %: C 85.63; H 14.37.

Combined dispersion spectrum, $\Delta\gamma$ cm$^{-1}$: 371 (2), 687 (8), 756 (0), 790 (0), 866 (2), 905 (0), 960 (0), 1025 (1), 1076 (0), 1112 (3b), 1130 (3), 1178 (1), 1224 (1), 1307 (7), 1397 (2), 1440 (10), 1450 (9), 1460 (9), 2852 (1), 2892 (3), 2937 (4), 2990 (4).

We obtained the same hydrocarbon by the slow distillation of 3-pentyl-5,5-dimethylpyrazoline.

B. p. 156-157°, $d_4^{20}$ 0.7514, $n^{20}D$ 1.4205, $MR_D$ 47.16; calc. 46.18.

The synthesis of 2-chloro-2-methyl-4-undecanone. The synthesis was carried out under conditions similar to those for the synthesis of 2-chloro-2-methyl-4-nonanone (see above) from capryl chloride and isobutylene. The boiling point of the capryl chloride was 85-95° (10 mm); literature data: b. p. 194-195° [15]. 292 g (97.7%) of 2-chloro-2-methyl-4-undecanone was obtained from 222 g of capryl chloride and 77 g of isobutylene. 152 g of the chloroketone was distilled under vacuum; two fractions were isolated: 1st, b. p. 87-110° (1 mm), 40 g; 2nd, b. p. 100-115° (1 mm) 62 g.

The 2nd fraction was 2-chloro-2-methyl-4-undecanone, $C_{12}H_{23}OCl$, $d_4^{20}$ 0.8861, $n^{20}D$ 1.4581.

The 1st fraction which consisted mainly of the ketone $C_{12}H_{22}O$ contained an admixture of the chloroketone $C_{12}H_{23}OCl$. The ketone $C_{12}H_{22}O$ was obtained with a yield of 55% by boiling the 1st fraction with a saturated solution of $K_2CO_3$.

B. p. 230-235°, $d_4^{20}$ 0.8495, $n^{20}D$ 1.4510, $MR_D$ 57.68; calc. 57.16. Found %: C 78.10; H 11.95. $C_{12}H_{22}O$. Calculated %: C 77.94; H 12.08.

The semicarbazone with a m. p. of 94-95° (from $C_2H_5OH$) was obtained.

Found %: N 17.68. $C_{13}H_{25}ON_3$. Calculated %: N 17.55.

The preparation of 3-heptyl-5,5-dimethylpyrazoline. The reaction was carried out under the conditions described above. 70 g of 2-chloro-2-methyl-4-undecanone in 40 ml of $C_2H_5OH$ and 24 g of hydrazine hydrate in 40 ml of $C_2H_5OH$ were taken. The reaction product was treated in the same way as in the previous experiments. 44 g (70%) of 3-heptyl-5,5-dimethylpyrazoline was obtained by distillation. On standing, the pyrazoline decomposed with the evolution of nitrogen.

B. p. 118-122° (1 mm), $d_4^{20}$ 0.7803, $n^{20}D$ 1.4613, $MR_D$ 61.776; calc. 61.694.

The catalytic decomposition of 3-heptyl-5,5-dimethylpyrazoline. The decomposition was carried out in a small copper flask in the presence of dry KOH and traces of 5% platinum on charcoal. 44 g of pyrazoline was used for the decomposition. The hydrocarbon distilled at 172-205°. The decomposition product of the base was treated in a similar manner to the previous experiments. 14.5 g (66.8%) of 1,1-dimethyl-2-heptylcyclopropane was obtained.

B. p. 200-201°, $d_4^{20}$ 0.7675, $n^{20}D$ 1.4278, $MR_D$ 56.06; calc. 55.41. The exaltation of 0.65 characterizes the presence of a three-membered ring in the hydrocarbon.

The analysis of the combined dispersion spectrum of the hydrocarbon indicated the presence of 95% of a hydrocarbon with a three-membered ring and approximately 5% alkene. The alkene was removed by oxidizing the hydrocarbon with a 1% solution of $KMnO_4$; 1,1-dimethyl-2-N-heptylcyclopropane remained.

B. p. 200-201°, $d_4^{20}$ 0.7681, $n^{20}D$ 1.4285, $MR_D$ 56.14; calc. 55.41. The exaltation of 0.73 characterizes the presence of a three-membered ring. Found %: C 85.60; H 14.42. $C_{12}H_{24}$. Calculated %: C 85.63; H 14.37.

Combined dispersion spectrum, $\Delta\gamma$ cm$^{-1}$: 367 (3), 585 (0), 627 (1), 683 (10), 768 (0), 864 (3), 893 (2), 952 (2), 1000 (1), 1027 (1), 1075 (2), 1112 (2), 1128 (3), 1244 (1), 1300 (10), 1390 (2), 1430 (10), 1440 (9), 1450 (9), 2850 (6), 2890 (4), 2934 (3), 2985 (5).

When 3-heptyl-5,5-dimethylpyrazoline is distilled in the absence of KOH and Pt a 69.3% yield of 1,1-dimethylheptylcyclopropane is obtained; it has the same constants as the hydrocarbon obtained by the catalytic decomposition of 3-heptyl-5,5-dimethylpyrazoline.

The preparation of 3,5,5-trimethylpyrazoline. 3,5,5-Trimethylpyrazoline was obtained from mesityl oxide and hydrazine hydrate.

B. p. 157-159°, $d_4^{20}$ 0.9002, $n^{20}D$ 1.4570, $MR_D$ 33.50; calc. 33.80. Literature data: b. p. 160.5° (764 mm), $d_4^{20}$ 0.8997, $n^{20}D$ 1.4566 [2].

The thermal decomposition of 3,5,5-trimethylpyrazoline. The decomposition was carried out in a catalytic horizontal oven filled with glass wool (25-50 cc). The pyrazoline base was fed to the oven from an automatic buret with a volumetric rate of 0.4. The liquid decomposition product was collected in a receiver cooled with ice and salt; the waste gas was collected in a gas holder. It was established that the base only begins to decompose at 340°, which is observable by the liberation of gas; intense decomposition takes place at 420-440°. 44 ml of base was passed through in 5 hrs; 41 ml was recovered. 1.5 ml of condensate was obtained from two experiments. 2.5 liters of gas was obtained. The condensate (1 ml) which was evidently a mixture of 2,3-dimethyl-2-butene and 2,3-dimethyl-1-butene was washed with 50% $CH_3COOH$, a 25% NaOH solution and water, dried with $CaCl_2$ and distilled.

B. p. 56.70°, $d_4^{20}$ 0.7057, $n^{20}D$ 1.4060, $MR_D$ 29.27; calc. 29.44. Literature data: 2,3-dimethyl-1-butene, b. p. 58°; 2,3-dimethyl-2-butene, b. p. 71-73° [16].

When the 56-70° fraction was brominated crystals of tetramethylethylene dibromide were obtained.

Analysis of the gas (in %): unsaturated hydrocarbons 1.9, ethylene 0.00, hydrogen 0.54, methane 71.50, nitrogen 26.06.

In conclusion, a number of observations may be made regarding the combined dispersion spectra which confirm the cyclic structure of the above-described hydrocarbons (I)-(III).
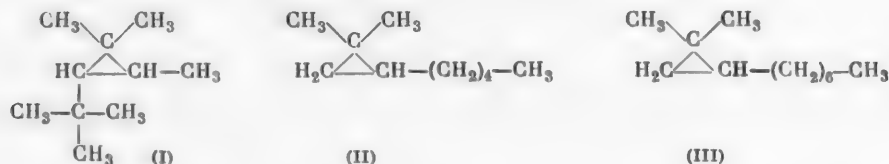


Lines in the 3000 $cm^{-1}$ region, characteristic of CH and $CH_2$ groups in a three-membered ring, are contained in these spectra. In addition, in the spectra of hydrocarbons (II) and (III) two frequencies (1112 and 1130 $cm^{-1}$) are observed which are found in the spectrum of 1,1,2-trimethylcyclopropane and probably belong to the frequencies of a ring somewhat reduced (in comparison with 1200 $cm^{-1}$) as a result of the presence of substituents. Only the frequency 1109 $cm^{-1}$ was definitely found in the spectrum of hydrocarbon (I). In the spectra of hydrocarbons (II) and (III) the frequency 1305 $cm^{-1}$ which belongs to the $CH_2$ group of an aliphatic chain is also found. As in the spectrum of 1,1,2-trimethylcyclopropane, intense lines in the 680-700 $cm^{-1}$ region, due to the presence of a gem-substituted carbon atom, are found in the spectra of these hydrocarbons.

The authors wish to express their thanks to V. P. Kuznetsov who took part in the investigation of the combined dispersion spectra.

## SUMMARY

1. The pyrazoline bases 3-N-pentyl-5,5-dimethyl- and 3-N-heptyl-5,5-dimethylpyrazolines, which when distilled at atmospheric pressure decompose with the liberation of nitrogen and cyclopropane hydrocarbons, were obtained for the first time from β-chloroketones. It was established that bases containing alkyl groups of normal structure in the molecule decompose far more readily than bases having branched alkyl groups.

2. 1,1-Dimethyl-2-N-pentylcyclopropane, 1,1-dimethyl-2-N-heptylcyclopropane and a mixture of 1,3-dimethyl-3-neopentylcyclopropane and 1,2,2-trimethyl-3-tert -butylcyclopropane were obtained for the first time.

3. The combined dispersion spectra of gem-substituted cyclopropane hydrocarbons were obtained and their characteristic frequencies were indicated.

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# THE INVESTIGATION OF TRITERPENES

## II. THE STRUCTURE OF ZEORIN

### A. A. Riabinin and L. G. Matiukhina

We established [1] that the triterpene alcohol zeorin with the composition $C_{30}H_{52}O_2$ (I, R = H) has an iso-propyl group adjoining the X ring and combined with a tertiary hydroxyl group. The other hydroxyl group, which has a secondary character, is located in one of the six-membered Y rings [2]. When zeorin is oxidized with chromic acid, acetone and a diketo acid $C_{27}H_{42}O_4$ are formed; this can be repreresented by one of two systems: (I, R = H) $\rightarrow$ (II) or (I, R = H) $\rightarrow$ (III).
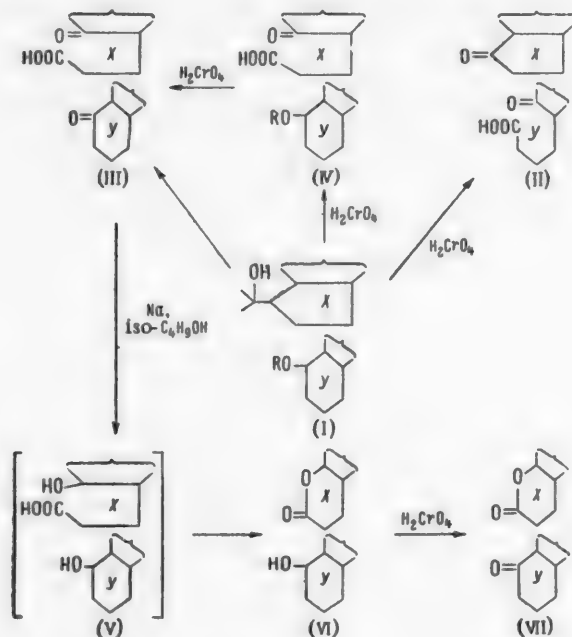


If the reaction takes place according to the latter system the oxidation of zeorin monoacetate (I, R = $CH_3CO$) should lead to the formation of an acetoxyketo acid (IV, R = $CH_3CO$) which after saponfication and further oxidation with chromic acid would be converted to a diketo acid (III). The experiment we carried out gave precisely these results. The carboxy and, therefore, the second ketone group of the diketo acid are, in consequence, formed by the decomposition of the X ring.

When the diketo acid (III) is reduced with sodium in isobutyl alcohol the dihydroxy acid (V) is formed which is converted to the oxylactone (VI), even during the process of formation. This oxylactone is readily oxidized by chromic acid to the ketolactone (VII). Both lactones are slowly saponified by the titration of their solutions in dioxane with caustic potash at 100°. The potassium salt obtained from the ketolactone was converted to the

crystalline silver salt. The hydroxyketo acid (IV, R = H) does not form a lactone even when acted on by a solution of sulfuric acid. It must, therefore, be assumed that the hydroxyl located at the point of rupture of the ring X takes part in the formation of the lactone ring. Zeorin, which is a saturated pentacyclic triterpene $C_{30}H_{52}O_2$ and has a side chain of three carbon atoms, must be formed of four six-membered and one five-membered ring. Comparing this fact with the readiness with which the dihydroxy acid (V) forms a lactone we may assume that the X ring in the zeorin molecule must be a five-membered one, while the ring in the lactone molecule must be six-membered. The isopropyl group must be connected to the X ring in the $\alpha$-position with respect to the connecting point of the rings, which is the usual structure in triterpene compounds of the lupane group.

The structure of the diketo acid and the lactones was confirmed by a spectroscopic investigation. Two absorption maxima, at 1700 and 1725 cm$^{-1}$, were discovered in the infrared spectrum of the methyl ester of the diketo acid (III). The first maximum corresponds to the keto group in the six-membered ring, the second maximum corresponds to the carbonyl of the ester group. The spectrum of the hydroxylacetone (VI) in the region of the carbonyl groups has only one absorption maximum corresponding to the carbonyl group in the six-membered ring of the lactone. In addition, it has a maximum at 3475 cm$^{-1}$, absent in the spectrum of the two other substances; this indicates the development of a hydroxyl group which takes part in the formation of an intramolecular hydrogen bond. Two maxima (at 1694 and 1743 cm$^{-1}$), associated with the keto group and the carbonyl group of the lactone ring, respectively,* are again found in the ketolactone (VII). The character of the keto groups agrees with the structure we assumed for the investigated compounds. The keto group located in the ring Y is inactive in zeorinone and does not condense with semicarbazide [2]; the diketo acid forms a monosemicarbazone [1] and the ketolactone does not give a condensation product with semicarbazide.

Investigating the crystalline ozonide, previously obtained [1], we established that as a result of catalytic hydrogenation it is converted to the diketone $C_{32}H_{52}O_4$. This determines the tertiary-tertiary character of the double bond of zeorinine.

By dehydrating zeorin in acetic acid solution in the presence of 5% sulfuric acid we obtained two diene hydrocarbons; it was not possible to identify these substances with known compounds.

## EXPERIMENTAL

1. Oxidation of zeorin monoacetate (I, R = CH$_3$CO). 8.54 g of zeorin monoacetate in 150 ml of acetic acid was oxidized at 42-44° with chromic acid obtained from 7.2 g of chromic anhydride. The solution was diluted with water, acidified with hydrochloric acid and the reaction products were extracted with ether. The ethereal solution was washed with water, the acid (IV, R = CH$_3$CO) was extracted with a solution of potash, precipitated with hydrochloric acid and saponified by boiling in a 25% methanol solution of caustic potash. As a result, 4.0 g of an indistinctly crystalline hydroxyketo acid (IV, R = H) was obtained. 1 g of this acid was oxidized in an acetic acid solution of 1 equiv. of chromic acid and the diketo acid (III) which melted at 244.5-245.5° (corr.) after recrystallization was obtained; the melting point of the methyl ester was 145.5-146.5° (corr.). The substances were identified by mixed melts with the corresponding compounds obtained previously [1]. The hydroxyketo acid (IV, R = H) did not form a lactone when its solution was heated in acetic acid containing 3% sulfuric acid for 40 min at 80°.

2. Hydroxylactone (VI). A solution of 8.95 g of diketo acid in boiling isobutyl alcohol was treated with sodium. The reaction mixture was washed with water and shaken with sulfuric acid after which crystallization of the hydroxylactone in the alcoholic layer commenced. The yield of the product was 5.5 g. After recrystallization from dioxane the m. p. was 230-231° (corr.).

Found %: C 78.14, 78.19; H 10.78, 10.95. $C_{27}H_{44}O_3$. Calculated %: C 77.83; H 10.64.

3. The ketolactone (VII). 4 g of the hydroxylactone was suspended in 400 ml of acetic acid and was oxidized at room temperature with chromic acid prepared from 1 g of anhydride. 2.5 g of ketolactone was obtained. After recrystallization from dioxane it was in the form of needles with a m. p. of 361.5° (corr.). A mixture with the hydroxylactone melted at 305-310°.

Found %: C 77.84, 77.85; H 10.50, 10.54. $C_{27}H_{42}O_3$. Calculated %: C 78.21; H 10.21.

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* All the substances were investigated in the form of suspensions in vaseline oil.

After the solution of the ketolactone and semicarbazide hydrochloride in pyridine had been allowed to stand for several days the initial substance was obtained. In a boiling dioxane solution the lactone slowly saponifies during titration with caustic potash. When a solution of the potassium salt obtained was mixed with an aqueous dioxane solution of silver nitrate the crystalline silver salt was precipitated.

Found %: Ag 20.16, 20.13. $C_{27}H_{43}O_4Ag$. Calculated %: Ag 19.63.

4. Acetoxydiketone. 3.20 g of the ozonide of acetylzeorine was hydrogenated in an ethereal solution with palladinized barium sulfate. 3.02 g of a crystalline substance was obtained. After several recrystallizations from alcohol it melted at 123-124° (corr.).

Found %: C 76.98, 76.80; H 10.65, 10.61. $C_{32}H_{52}O_4$. Calculated %: C 76.75; H 10.47.

The diketone is not oxidized when acted on by chromic acid in acetic acid solution at room temperature for several hours. It forms a disemicarbazone with a m. p. of 220° (corr.).

Found %: N 13.67, 13.72. $C_{34}H_{58}O_4N_6$. Calculated %: N 13.67.

5. Diene hydrocarbons. 14.7 g of zeorin was heated at 100° in 300 ml of acetic acid, containing 5 ml of sulfuric acid, for 50 min. After the mixture had cooled, 7.7 g of a felt-like mass of fine needles was filtered. After recrystallization from acetone or acetic acid the substance melted at 181-182° (corr.), $[\alpha]_D$ 47.6° (c 4.22).

Found %: C 87.95, 87.92; H 12.24, 12.26. $C_{30}H_{48}$. Calculated %: C 88.16; H 11.84.

The tarry mass which precipitated out when the acetic acid mother liquor was diluted with water was chromatographed from petroleum ether on aluminum oxide; a hydrocarbon with a m. p. of 137-143° was obtained. The substance remained unchanged with repeated chromatography and recrystallization.

Found %: C 87.87, 87.85; H 11.77, 11.76. $C_{30}H_{48}$. Calculated %: C 88.16; H 11.84.

It should be noted that the analysis of some of the compounds obtained from zeorin by various authors, including those we obtained in this work, leads to the formula $C_{30}H_{50}O_2$ for zeorin. The analysis of the great majority of compounds, however, agrees with the formula $C_{30}H_{52}O_2$. We carried out numerous analyses of zeorin, purified by various methods, and confirmed the latter formula. In giving the results of the analyses of the substances investigated by us, we therefore compare them with the theoretical results on the basis of this formula.

## SUMMARY

1. It was established that the triterpene alcohol zeorin has a five-membered ring to which an isopropyl group is joined in the $\alpha$-position with respect to the connecting point of the ring and the neighboring ring. This structure is found in derivatives of lupane. The formation of the previously-described diketo acid takes place by the rupture of this five-membered ring.

2. By splitting the ozonide of acetylzeorinine a ketone was obtained, indicating the tertiary-tertiary character of the double bond of zeorinine.

3. By dehydrating zeorin, two diene hydrocarbons distinct from the initial substances were obtained.

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* Original Russian pagination. See C. B. translation.

# THE CONDENSATION PRODUCTS OF L-EPHEDRINE AND
# D-PSEUDOEPHEDRINE WITH ACETONE

L. G. Matsova and A. S. Labenskii

As is known, aminoethanols react with aldehydes and ketones forming condensation products which are derivatives of oxazolidines [1]. In the case of ephedrine and pseudoephedrine only condensation products of these alkaloids with benzaldehyde are known [2].

Working with D-pseudoephedrine we found that the mother liquor obtained in the recrystallization of D-pseudoephedrine from acetone contains an unknown substance. We isolated the latter and characterized it. The compound obtained was a colorless oily product which readily distills under vacuum. The salts of this substance were also prepared and characterized. We then obtained the same substance by boiling D-ephedrine with acetone. It was found that the presence of alkaline activated charcoal appreciably accelerates the reaction.

On the basis of the method of preparation of the substance and also from the established elementary composition and the determination of the molecular weight of the hydrochloride of the substance it may be assumed that the substance is an oxazolidine derivative formed by the condensation of D-pseudoephedrine with acetone.

$$C_6H_5-CH-CH-CH_3 + (CH_3)_2CO \longrightarrow C_6H_5-CH-CH-CH_3 + H_2O$$
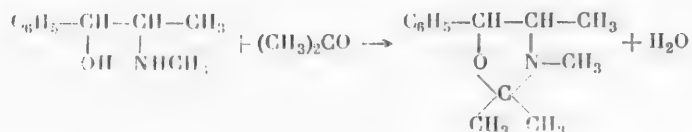
All the data we obtained confirmed this assumption. For instance, as a result of the acid hydrolysis of the compound obtained, D-pseudoephedrine was isolated. This fact agrees with previous information [1, 3], according to which, as a result of similar hydrolysis, oxazolidine derivatives readily split up with the formation of the corresponding aminoethanols.

The investigation of the infrared spectrum of the substance showed the absence of an absorption maximum in the 3520-3110 cm$^{-1}$ region, characteristic of a hydroxyl group, and also in the 3500-3100 cm$^{-1}$ and 1580-1510 cm$^{-1}$ regions, characteristic of a secondary amino group. The infrared spectrum of D-pseudoephedrine has a corresponding absorption maximum.

The determination of the value of the molecular refraction also confirmed the above-mentioned assumption regarding the structure of the substance obtained, which in accordance with the work of Hückel [4] and Close [5] can be determined as D-trans-2,2,3,4-tetramethyl-5-phenyloxazolidine.

In view of the fact that certain compounds of similar structure possess physiological activity [6], the hydrochloride of the compound we obtained was subjected to a corresponding investigation. It was found that this compound has weak adrenomimetric and spasmolytic effects compared with already-known remedies.*

By analogy with the above-mentioned reaction we condensed L-ephedrine with acetone. The mixture was boiled until a constant angle of rotation of the reaction mass was obtained. As a result of the reaction we obtained

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* The pharmacological investigation of the substance was carried out by Iu. I. Syrneva.

an oily substance which distilled under vacuum. The substance became crystalline on standing in a refrigerator. The ultimate analysis and also the result of acid hydrolysis which leads to the formation of L-ephedrine proves that the compound we obtained is D-cis-2,2,3,4-tetramethyl-5-phenyloxazolidine.

We also obtained and characterized the picrate of D-cis-2,2,3,4-tetramethyl-5-phenyloxazolidine. The hydrochloride and perchlorate were also obtained. It was impossible to purify the latter substances for analytical purposes because of their instability.

It should be noted that it requires a considerably longer time (25 hrs) to complete the condensation reaction of L-ephedrine and acetone than for the analogous reaction with D-pseudoephedrine (5 hrs). This difference can be explained by the different spatial structure of these compounds as a result of which the condensation of ephedrine encounters steric hindrance [7].

## EXPERIMENTAL

1. 20 g of D-pseudoephedrine with 70 ml of acetone and 0.5 g of alkaline activated charcoal were boiled with a reflux condenser on a water bath for 5 hrs. After the solution had been filtered from the charcoal the filtrate was evaporated. The oil remaining was distilled under vacuum. The yield was 22.4 g (90%).

B. p. 117° at 8 mm, $[\alpha]_D$ +34.92°, $d_4^{20}$ 0.9823, $n^{18.5}D$ 1.5085, $MR_D$ 62.19; calc. 62.016. Found %: C 75.83; H 9.20; N 7.07. $C_{13}H_{19}ON$. Calculated %: C 76.06; H 9.33; N 6.82.

The hydrochloride was obtained by mixing ethereal solutions of the base and hydrogen chloride.

After it had been recrystallized twice from a mixture of acetone and methanol, the m. p. was 181-182°, $[\alpha]_D$ +46.9° (c 9.2; water). Found %: C 64.67; H 8.51; N 5.77; Cl 14.50. M (by Rast's method) 233; M (by titration) 240.2. $C_{13}H_{20}ONCl$. Calculated %: C 64.71; H 8.28; N 5.80; Cl 14.67. M 241.76.

The picrate was obtained by mixing alcoholic solutions of the base and picric acid.

After the picrate had been recrystallized from a mixture of acetone and methanol, the m. p. was 142-143° (decomp.), $[\alpha]_D$ -41.3 (c 4.6; acetone). Found %: C 52.69; H 5.22; N 13.14. $C_{13}H_{19}ON \cdot C_6H_3O_7N_3$. Calculated %: C 52.70; H 5.11; N 12.90.

2. 5.52 g of the trans-substituted oxazolidine and 50 ml of a 20% alcoholic solution of hydrogen chloride were boiled with a reflux condenser on a water bath for 3.5 hrs. After the evaporation of solution, the addition of water to the residue, treatment with 10% NaOH and extraction of the bases with ether, a mixture of oil and crystals was obtained. The latter were filtered, washed with a small amount of acetone and then dried. The yield was 1.2 g. The crystals were identified by direct comparison with D-pseudoephedrine.

3. 16.15 g of L-ephedrine was boiled with 70 ml of acetone and 0.5 g of alkaline activated charcoal for 25 hrs with a reflux condenser on a water bath. After the charcoal had been removed the filtrate was evaporated. The oil which remained was distilled under vacuum. The yield was 17.0 g (85%).

B. p. 116° at 7.5 mm, m. p. 26-34° (in a sealed capillary), $[\alpha]_D$ +19.1° (c 7; acetone). Found %: C 75.73; H 9.32; N 6.95. M (by titration) 206.5. $C_{13}H_{19}ON$. Calculated %: C 76.06; H 9.33; N 6.82. M 205.36.

The picrate was obtained by adding an alcoholic solution of picric acid to the hot alcoholic solution of the base.

M. p. 180.5-182°, $[\alpha]_D$ -64.3° (c 0.4; acetone). Found %: C 52.45; H 5.13; N 12.79. $C_{13}H_{19}ON \cdot C_6H_3O_7N_3$. Calculated %: C 52.70; H 5.11; N 12.90.

The perchlorate was obtained by adding hydrochloric acid to an alcoholic solution of the base. The m. p. was 183-184°, $[\alpha]_D$ -17.75° (c 1; acetone). After recrystallization from anhydrous alcohol the m. p. was 174-176°; when heated under vacuum the substance turned pink.

The hydrochloride was obtained by mixing an ethereal solution of the base and an alcoholic solution of hydrogen chloride. The m. p. was 151-164°. After recrystallization from acetone-methanol mixture the m. p. was 153-164°, $[\alpha]_D$ -38.24° (c 1.4; water). A crystalline product was obtained from the mother liquor.

4. A solution of 1 g of cis-substituted oxazolidine in 10 ml of alcohol was boiled with 10 ml of 17% alcoholic hydrochloric acid with a reflux condenser on a water bath for 3.5 hrs. A crystalline precipitate was obtained when the solution was cooled. The weight was 0.42 g. The identity of the precipitate was established by a mixed melt with L-ephedrine hydrochloride (no depression) and by the value of the specific rotation.

## SUMMARY

The condensation products of L-ephedrine and D-pseudoephedrine with acetone and their salts were obtained for the first time.

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# HORMONES OF THE THYROID GLAND AND THEIR ANALOGS

## IV. THE SYNTHESIS OF DESAMINO ANALOGS OF BETAZINE (β-DIIODOTYROSINE)

### N. N. Suvorov, L. M. Morozovskaia, and A. A. Dudinskaia

In previous communications [1] we described the synthesis of a new antithyrotropic preparation "betazine" (β-diiodotyrosine) and a number of β-amino acids which are isomers and analogs of the latter. To investigate the relationship between the physiological action and the chemical structure it was of interest to study the activity of the corresponding substituted propionic acids, i. e., compounds without an amino group in the side chain.

We synthesized β-(4-hydroxy-3,5-diiodophenyl) propionic acid by the following system: p-methoxycinnamic acid (I) was hydrogenated over Raney nickel, the product (II) obtained was demethylated by boiling with hydrobromic acid and the p-hydroxycinnamic acid (III) was iodized by Lugol's solution in ammonia.
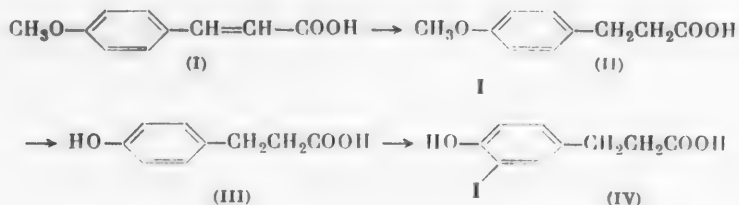


It must be pointed out that β-(4-hydroxy-3,5-diiodophenyl) propionic acid has been described in literature and was obtained by the iodination of p-hydroxyhydrocinnamic acid (III) with iodine in a solution of caustic soda [2].

The method we proposed for obtaining p-hydroxyhydrocinnamic acid is original.

We also obtained 3-hydroxy- and 3-aminohydrocinnamic acids by the hydrogenation of 3-hydroxy- and 3-nitrocinnamic acids, respectively, over Raney nickel. Their iodination was carried out according to literature data [3, 4].

The physiological activity of the compounds obtained will be reported elsewhere.

## EXPERIMENTAL

p-Methoxyhydrocinnamic acid (II). 15.5 g of p-methoxycinnamic acid (I) was hydrogenated in 77 ml of ethyl alcohol over Raney nickel (~ 3 g) at 30 atmos and 80°. The solvent was distilled off under vacuum, the residue was crystallized from a mixture of 45 ml of alcohol and 60 ml of water, employing activated charcoal to decolorize the solution. 13.8 g of a product with a m. p. of 102-103° was obtained. It was possible to obtain a further 0.5 g of fairly pure acid from the mother liquors. The total yield was 91%. Literature data: m. p. from 101-104° [5].

p-Hydroxyhydrocinnamic acid (III). 7 g of p-methoxycinnamic acid (II) was boiled with stirring with 35 ml of 40-48% hydrobromic acid until the oil which was initially formed had completely dissolved (about 4 hrs). The solution was then cooled and the precipitated p-hydroxyhydrocinnamic acid was filtered through a glass filter.

It was crystallized from 7 ml of 10% aqueous alcohol with activated charcoal. The yield was 5.56 g (86%). The m. p. was 126.5-129°. Literature data: m. p. from 128-130° [5].

β -(4-Hydroxy-3,5-diiodophenyl) propionic acid (IV). A solution of 6.7 g of iodine and 5.7 g of potassium iodide in 26 ml of water was added to a solution of 2 g of p-hydroxyhydrocinnamic acid in 14 ml of 12% aqueous ammonia at 5° over a period of 30 min. After 1 hr the excess iodine was removed by adding sodium bisulfite and the iodine-containing acid was precipitated with hydrochloric acid. After 3 crystallizations from aqueous alcohol 2.02 g (40%) of a substance with a m. p. of 161-162° was obtained (Bougault [2] indicates a m. p. of 162°).

Found %: I 60.57. $C_9H_8O_3I_2$. Calculated %: I 60.70.

β -(3-Hydroxy-2,4,6-triiodophenyl) propionic acid. A mixture of 12.4 g of m-hydroxybenzaldehyde, 18.5 g of malonic acid, 19 ml of pyridine and several drops of piperidine was boiled for 4.5 hrs and when cool it was poured into 105 ml of hydrochloric acid (1 : 2). The precipitate deposited was filtered, washed with water and dried. 14.8 g (89%) of m-hydroxycinnamic acid with a m. p. of 191-192° (from aqueous methanol) was obtained.

9.58 g of this acid was hydrogenated over Raney nickel in 96 ml of ethyl alcohol at 30 atmos and 80°. 7.45 g (77%) of m-hydroxyhydrocinnamic acid was obtained. The latter was iodized with iodine monochloride in glacial acetic acid. The m. p. was 225-226° (from a 1 :1 mixture of acetone and water). Literature data: m. p. 225-226° [3].

β -(3-amino-2,4,6-triiodophenyl) propionic acid was obtained in similar manner from m-nitrobenzaldehyde.

## SUMMARY

1. Desamino analogs of betazine were prepared for pharmacological purposes: β -(4-hydroxy-3,5-diiodo)-, β -(3-hydroxy-2,4,6-triiodo)- and β -(3-amino-2,4,6-triiodo) phenylpropionic acids.

2. A new convenient method of preparing p-hydroxyhydrocinnamic acid was proposed.

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[5] Beilst. 10, 245.

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** In Russian.

# THE SPECTROPHOTOMETRIC INVESTIGATION OF THE REACTION OF CHLOROPHYLL WITH FERRIC CHLORIDE

S. S. Butsko and B. Ia. Dain

It is known that considerable amounts of iron salts are contained in the chlorophyll-bearing plastids of the green leaves of plant organisms [1]. Certain data indicate the presence of a close bond between these salts and chlorophyll and its protein carrier [2]. In this connection the problem of the nature of the chemical reactions which can take place in corresponding associates is of interest.

It is natural to expect that under favorable circumstances the iron ions must displace magnesium from the chlorophyll nucleus with the formation of a hemin structure. The data of Barnes and Dorough [3], who observed a number of reactions of the displacement of one metal by another in metallotetraphenylporphins, are particularly in favor of such an assumption. The investigation of processes of this type in chlorophyll is of particular importance in connection with the interesting optical properties of hemin-like analogs of chlorophyll, making probable their participation in the photochemical phase of photosynthesis [4]. On the other hand, Rabinowitch and Weiss [5] gave a number of data which suggested that in alcoholic solution trivalent iron ions reversibly oxidize chlorophyll in darkness with the formation of a hypothetical oxidized form according to the system.

$$Fe^{+++} + Chl \rightleftarrows Fe^{++} + oxyChl*. \tag{1}$$

The presence of such a reaction would signify that even in the dark an unstable product with a high oxidation potential is formed in the leaf, this product also being capable of acting as an important factor for initiating the development of the oxidation branch of the photosynthesis reaction.

The fact that the reaction of chlorophyll with ferric chloride in alcoholic solutions is complicated by side reactions which complicate the explanation of the nature of the main reaction [6] should, however, be taken into consideration. The pheophytinization of chlorophyll, which is observed in alcoholic solutions, is due to the hydrogen ions formed during the solvolysis of iron salts, and complicates the investigation markedly. As a result of this, the reversible reaction postulated by Rabinowitch and Weiss on the basis of spectral data obtained for alcoholic solutions cannot be considered as proven.

The present article gives the results of the spectrophotometric investigation of the reaction of chlorophyll with anhydrous ferric chloride in diethyl ether and acetone, solvents in which the effect of the pheophytinization of chlorophyll is practically excluded.

## EXPERIMENTAL

The reaction vessel. Preliminary experiments indicated that in air (to be more precise, in the presence of dissolved oxygen) the reaction between ferric chloride and chlorophyll is complicated by side reactions. The investigation of the reactions which interested us was, therefore, carried out under high vacuum.

The investigated reaction and also the preceding operations to remove traces of air from the solutions and mix them were carried out in a seamless glass vessel connected to a high-vacuum installation (Fig. 1). Apart
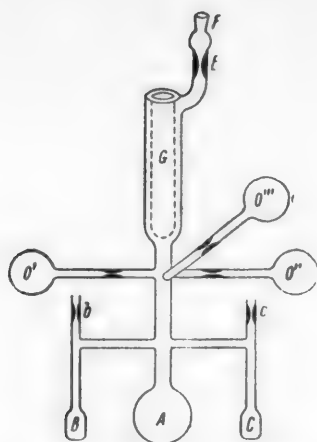
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* Oxychl = oxychlorophyll.
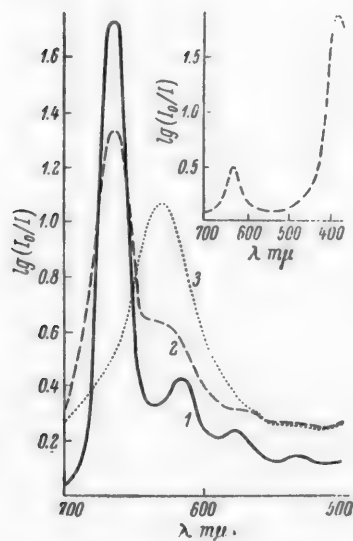
Fig. 1. Reaction vessel. Explanation in text.



Fig. 2. Changes in the spectrum of an ethereal solution of chlorophyll a during its reaction with $FeCl_3$. Absorption curves: 1) of the initial solution; 2) after 18 hrs; 3) after 6 days. In the upper part — the absorption curve of an alcoholic solution of the reaction product of chlorophyll and $FeCl_3$.

from the main receptacle A in which the chlorophyll solution was placed, the vessel had branch pieces B and C for the ferric chloride and other reagents and also cuvettes O', O" and O''' for spectrophotometric measurements. The cuvettes, filled under vacuum, were sealed off from the vessel and the solutions contained in it were subjected to photometry in an SF-4 spectrophotometer.

Preparations. Chlorophyll a was obtained from dry nettle leaves according to method [7] and was separated from components b by chromatography in a column with anhydrous sugar powder. The purity of the pigment was checked in each instance by the analysis of its absorption spectrum. The solvents were purified by methods given in the book [8] and were distilled again before the experiment. Anhydrous ferric and ferrous chloride which were obtained by usual methods and kept under vacuum in sealed ampules were used in the experiments.

Experimental procedure. 15 ml of a solution of chlorophyll with a concentration of $\sim 10^{-5}$ mole was introduced into the receptacle A and 1 ml of solvent and several small crystals of anhydrous $FeCl_3$ were added to the branch piece B. The branch piece was then sealed off at the constriction b. The vessel was connected to the high-vacuum installation by means of the ground-in joint F. Liquid air was poured into the trap G to prevent the vapors of the solvent from entering the vacuum system. After the solutions had been completely degassed and a high vacuum had been established, the vessel was sealed at the constriction E. Because the solvent from the lateral branch piece passed into the receptacle during the process of evacuation of the system toward the end of pumping, the ferric chloride was present in the form of a solid film on the walls of the container B. After part of the solution had been led off to the cuvette for spectrophotometric measurements and it had been sealed off from the system, the lateral branch piece was immersed in liquid air for several minutes, as a result of which, part of the solvent distilled from it into the receptacle A. The solution of ferric chloride obtained after defreezing was poured into the receptacle and was carefully shaken. The cuvettes were filled with the solution obtained, then they were sealed off from the vessel and subjected to photometry at specific periods. When it was necessary to know the exact concentrations of the solutions of salts added, appropriate, previously-prepared solutions were introduced instead of crystals in the branch piece B. The volume of liquid in the receptacle after mixing was always made up to the same level. The addition of the other reagents ($FeCl_2$, $CaCl_2$, NaCl) was carried out by a similar method via the branch piece C.

The reaction of chlorophyll with ferric chloride in a solution of ether takes place extremely slowly. The first changes in the spectrum, consisting in a certain reduction in the intensity of the red absorption band of chlorophyll at 662 m$\mu$ and the appearance of a band of the reaction product at 630 m$\mu$, initially of low intensity, is only noted several hours after the mixing of the solutions (Fig. 2).

The intensity of this band increases slowly with simultaneous weakening of the absorption bands of chlorophyll. The latter disappear completely only after 6-7 days. After the reaction had been completed the products were brought into solution in chloroform. The separated chloroform layer was repreatedly washed with water until iron salts had been completely removed and it was then evaporated to dryness. After being carefully dried under

vacuum the dry residue was dissolved in alcohol. The spectrum of the alcoholic solution of the product (shown in the upper part of Fig. 2) has two intense bands at 630 and 385 mμ and, in contrast to the spectrum of chlorophyll, does not contain vibrational bands of low intensity. As regards the position of the maxima and the ratio of their intensities, this spectrum coincides completely with the spectrum of pheophytin iron-III,* previously investigated [4]. From these data it follows that as a result of the reaction of chlorophyll and ferric chloride there is an intense displacement of magnesium by iron, which may be summarily expressed by the equation

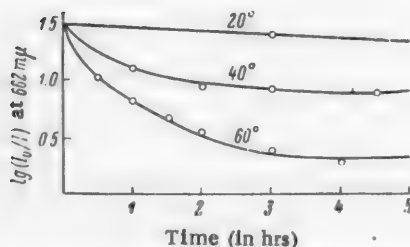$$MgPh + FeCl_3 \mapsto FeClPh + MgCl_2. \tag{2}$$



Fig. 3. The influence of temperature on the rate of introduction of iron into the nucleus of chlorophyll.
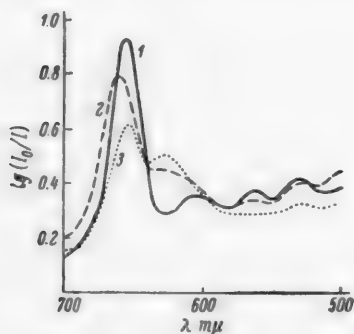


Fig. 5. The influence of oxygen on the process of the introduction of iron into the chlorophyll nucleus. Absorption curves: 1) of the gray intermediate product, 2) after the admission of air, 3) after keeping in air for 10 days.



Fig. 4. Changes in the spectrum of an acetone solution of chlorophyll a during its reaction with FeCl_3. Absorption curves: 1) of the initial solution of chlorophyll a, 2) directly after the introduction of FeCl_3 , 3) after 5 days.

This was confirmed by additional experiments in which the reaction product was isolated in the pure form and ashed. Iron and chlorine were found in the ash of the product and the absence of magnesium was established. The exposure of an alcoholic solution of the product to light leads to its reduction (the appearance of bands at 655 and 410 mμ and the disappearance of the bands at 630 and 385 mμ), which is characteristic for pheophytin iron -III [4].

The slow course of the reaction is evidently associated with the high energy of activation. In fact, an increase in temperature markedly accelerates the reaction, as follows from a comparison of the velocity curves for 20, 40 and 60° given in Fig. 3.

The course of the reaction in acetone solution shows interesting features which are essential for understanding its mechanism. In this instance also, the end product is pheophytin iron-III. In this solvent, however, fundamental spectral charges are detected immediately after the introduction of the iron salt (Fig. 4). The green solu-
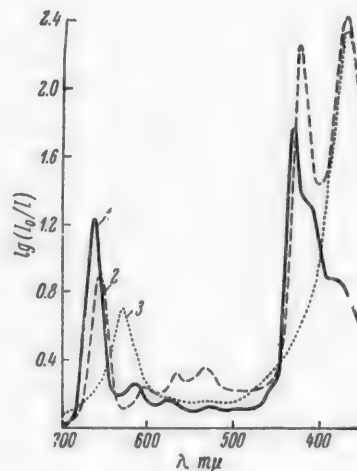
* Pheophytin iron, the product of the substitution of the central atom of magnesium in the chlorophyll nucleus by iron, exists in oxidized (FeX complexes where X is hydroxyl or an acid residue) and reduced forms (Fe complex). The oxidized form of this derivative of chlorophyll and its analogs was investigated in [9, 10]. The reduced product was obtained by the photochemical reduction of the oxidized form [4]. The abbreviations MgPh, FeClPh, FePh, where Ph is the organic nucleus of chlorophyll without metal, will be used subsequently for chlorophyll and these derivatives, respectively.
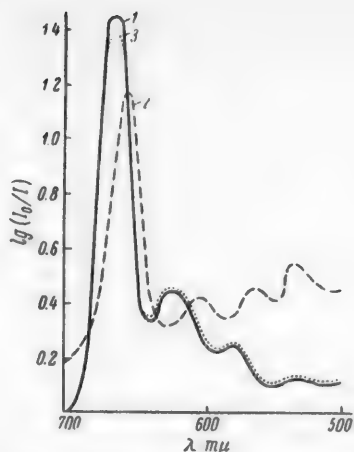
Fig. 6. The influence of additions of CaCl₂. Absorption curves: 1) of the initial solution of chlorophyll a in acetone; 2) after the introduction of FeCl₃; 3) after the addition of CaCl₂.
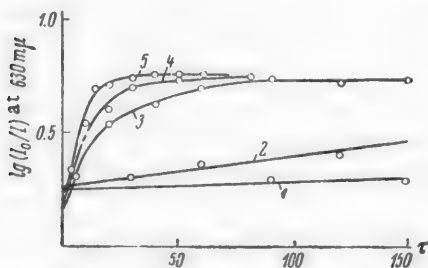


Fig. 8. The influence of additions of FeCl₂ on the rate of introduction of iron into the chlorophyll nucleus. Curves of the variation of $\log(I_0/I)$ for $\lambda = 630$ m$\mu$ with respect to time (in min): 1) without additions of FeCl₂. Conc. of FeCl₂ (in mole/liter): 2) $6 \cdot 10^{-6}$, 3) $1.8 \cdot 10^{-5}$, 4) $2.4 \cdot 10^{-5}$, 5) $3 \cdot 10^{-5}$.



Fig. 7. The influence of additions of CaCl₂ on the intensity of the absorption maxima of regenerated chlorophyll and pheophytin iron. 1) Absorption of regenerated chlorophyll at 662 m$\mu$; 2) Abs. of the product formed in the reaction, 630 m$\mu$; $\tau$) time (in hrs), elapsed from the moment of the formation of gray product until the introduction of CaCl₂.

tion becomes grayish. The red absorption band of chlorophyll (662 m$\mu$) is considerably reduced and is somewhat displaced toward the shortwave side, up to 655 m$\mu$. Other bands appear simultaneously: bands of low intensity at 605, 565, and 535 m$\mu$ and two very intense bands at 420 and 370 m$\mu$. The spectrum of the gray product is fairly stable and is accurately reproduced in all the experiments. On long standing the intensity of its characteristic absorption bands is gradually reduced. Bands of pheophytin iron-III appear simultaneously. The reaction proceeds somewhat more rapidly than in ethereal solutions. It is markedly retarded, however, if the solution containing the gray product is brought into contact with air. In this instance it is not possible to observe an appreciable increase in the intensity of the absorption band at 630 m$\mu$, belonging to pheophytin iron, even after 10 days (Fig. 5); this indicates the extremely marked retarding influence of oxygen on the process of the introduction of iron into the center of the porphin nucleus.

The initial changes found in the spectrum of chlorophyll as a result of the introduction of ferric chloride are reversible. The initial state may be re-established by adding chlorides (solutions of NaCl, CaCl₂, etc.) (Fig. 6). Complete regeneration of chlorophyll is, however, attained only when these salts are introduced immediately after the formation of the gray product. The regeneration of the chlorophyll is otherwise found to be incomplete and a maximum at 630 m$\mu$, belonging to pheophytin iron, appears simultaneously in the spectrum. The intensity of this maximum is greater the longer the time from the moment of formation of the gray product to the introduction of the chloride. The reverse relationship is found for the red maximum of regenerated chlorophyll (Fig. 7). A considerable degree of regeneration of chlorophyll can, nevertheless, be noted even after 20-25 hrs. This fact indicates that the gray intermediate product is not labile and has a very long life.

From the data given it follows that the investigated process in acetone solution takes place in two stages. The first of these, associated with the formation of the intermediate product, is reversible. The second, in which the end product is formed, is irreversible. The process may be represented according to the following system:
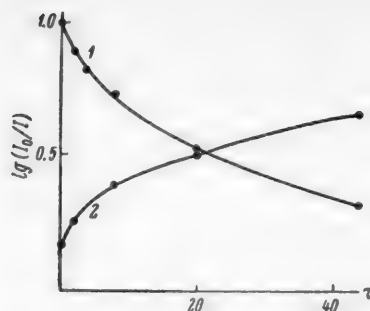
$$\text{FeCl}_3 + \text{MgPh} \rightleftarrows \text{Intermediate product} \longrightarrow \text{FeClPh} + \text{MgCl}_2. \tag{3}$$

Catalysis by iron ions.   As we saw above, the action of NaCl and CaCl$_2$ on the gray intermediate product displaces the primary stages of the process in system (3) to the left. The addition of FeCl$_2$ has the same action. If equivalent amounts of anhydrous FeCl$_3$ and FeCl$_2$ are introduced in the solution of chlorophyll from the very start, the formation of the gray product is not noted at all because the equilibrium is completely displaced to the left. Ferrous chloride also has a specific action on the course of the process.   The   addition   of   CaCl$_2$   and NaCl, which regenerates chlorophyll, simultaneously retards the further progress of the process of the introduction of iron into the chlorophyll nucleus; ferrous chloride, on the other hand, markedly accelerates this process. In the investigated instance, when equivalent amounts of bivalent and trivalent iron salts are used, complete conversion of chlorophyll to pheophytin iron is attained after 10-15 min. The catalytic influence of FeCl$_2$ is already clearly indicated in those instances when it is added in negligibly low concentrations and increases very markedly with the increase of its concentration in the solution. This is illustrated by data on the course of the reaction during the period of various additions of ferrous chloride, given in Fig. 8.

## DISCUSSION OF RESULTS

From the data obtained it follows that the reaction of chlorophyll with ferric chloride leads to the displacement of magnesium from the chlorophyll by iron and the formation of pheophytin iron. No side reactions occur in this process. The hypothesis of the reversible oxidation of chlorophyll to its oxy form, advanced in previous investigations [5], is therefore not confirmed. In the interpretation of the mechanism of the reaction we take as our basis the assumption that it is effected between molecules of chlorophyll and molecules of ferric chloride or its ions. The latter is assumed for acetone solutions in which the ionic dissociation is fairly strongly expressed. A purely ionic interpretation of the exchange reaction observed must obviously be rejected. It is hardly possible to admit an appreciable dissociation of the chlorophyll molecules in a nonaqueous solvent. At the same time if such an admission is made it is impossible to explain a number of the facts observed, in particular the catalysis of the process by bivalent iron ions and also the effect of the regeneration of chlorophyll as a result of the addition of chlorides.

The problem of the nature of the gray product formed immediately after the introduction of ferric chloride in a solution of chlorophyll in acetone is very essential for understanding the mechanism of the process. The formation of this product is not associated with any significant disturbances in the structure of the porphin nucleus of chlorophyll, this being indicated by the spectrum which is typical of dihydroporphin derivatives. This product is very stable, which is confirmed by its long life. On the other hand, its formation is an essential stage of the reaction, ensuring the necessary conditions for its further progress. In an ethereal solution where the gray product is not formed the reaction takes place extremely slowly. In acetone, however, particularly in the presence of Fe$^{++}$ ions, it can take place very rapidly. This justifies the consideration of the gray product as the active intermediate reaction product.

The primary changes observed in the spectrum of chlorophyll as a result of the introduction of ferric chloride are the result of the formation of Fe(MgPh)$^{+++}$ ions for which the conditions are favorable in acetone solutions. These particular complex ions are carriers of those properties which were noted in the gray product. In fact, as a result of the formation of such complexes the iron ion inevitably established a bond with the quaternary nitrogen atoms of the chlorophyll nucleus. This must lead to the labilization of the bonds of these atoms with magnesium which also creates favorable conditions for its displacement from the molecule. It is precisely this which determines the role of the gray product in the development of the reaction. The polarization effects which must take plase as a result of the reaction of the Fe(MgPh)$^{+++}$ ions with the chlorine ions must lead to the decomposition of these complexes and the regneration of chlorophyll. This explains the influence of chlorides in the first stage of the process which was observed in our work.

The labilization of the bonds between magnesium and the central nitrogen atoms of the chlorophyll nucleus which is evidently attained in the complex Fe(MgPh)$^{+++}$ ions is a necessary but insufficient condition for the realization of the reaction. This is indicated by its fairly slow progress in the absence of Fe$^{++}$ ions. Here it is possible that certain steric factors also play a part because the chlorine atom must be attracted into the porphin nucleus as well as trivalent iron. The catalytic influence of Fe$^{++}$ ions is evidently associated with the fact that they first enter the labilized nucleus of chlorophyll, which is represented by the equation (4a)

$$Fe(MgPh)^{+++} + Fe^{++} \longrightarrow FePh + Mg^{++} + Fe^{+++} \tag{4a}$$
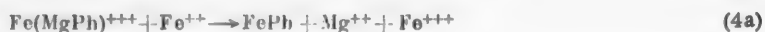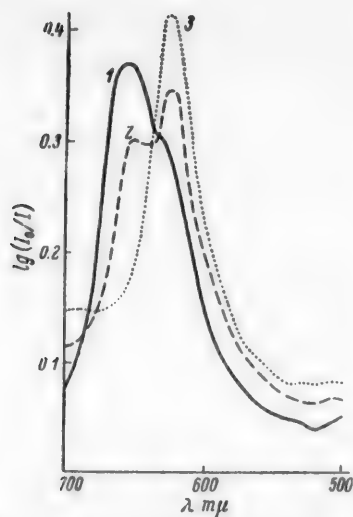
Fig. 9. The absorption curves for the product of the introduction of Fe into the chlorophyll nucleus showing the influence of the photoreduction of the original $FeCl_2$ solution. Irradiation of the $FeCl_2$ solution (in hrs): 1) 5, 2) 2, 3) no irradiation.

The formation of the end product takes place as a result of the oxidation of reduced pheophytin iron by iron chloride

$$FeCl_3 + FePh \longrightarrow FeClPh + FeCl_2 \qquad (4b)$$

a reaction which as indicated by separate experiments, takes place extremely slowly.*

The particular feature of the proposed reaction system** consists in the fact that it leads to a chain mechanism in connection with the regeneration of ferrous chloride in stage (4b). Even very low concentrations of $Fe^{++}$ ions, therefore, cause a considerable displacement effect of magnesium by iron from the chlorophyll nucleus. From all the data the intense retardation of the reactions by oxygen which was observed in our work is associated with the rupture of the reaction chains which takes place as a result of the oxidation of the $Fe^{++}$ ions.*** To obtain a final confirmation of the reaction system it is extremely important to realize the individual stage (4a). This is complicated, however, by the fact that in the presence of ferric chloride the second stage (4b) also proceeds immediately. In the absence of it, however, the required conditions for the reaction (4a) to take place are not present. In the supplementary experiments described below conditions under which only traces of ferric chloride were present in the reaction mixture of chlorophyll and ferrous chloride were ensured; it was therefore possible to detect the product of the first stage of the reaction.

Ferrous chloride which had been kept for some time in air was used for the experiments. In two of the three experiments carried out (Fig. 9) a solution of the salt was first exposed to irradiation by a mercury quartz lamp in order to partially reduce the trivalent iron formed as a result of the oxidation of the $Fe^{++}$ ions.

As may be seen from the data in Fig. 9, in both experiments the reaction with chlorophyll led to the formation of two of its iron derivatives: pheophytin iron-II (absorption maximum at 655 mμ[4]) and pheophytin iron-III (absorption maximum at 630 mμ). Since the content of $Fe^{+++}$ ions (and, therefore, $Fe(MgPh)^{+++}$ ions also) was extremely small, the introduction of iron was an extremely slow process in both experiments. The end state of the system in the experiment with a high content of trivalent iron was attained far more rapidly (in 6 hrs), however, whereas when the period of irradiation was less, the reaction took a day.

In the third experiment, in which the solution of $FeCl_2$ was not irradiated the reaction took place in 40 min and led to the formation of a single product, pheophytin iron-III.

We feel that these experiments give a convincing and very graphic proof of the reality of the above-proposed reaction system. This system is also applicable for those instances when the reaction proceeds without special additions of ferrous chloride. The traces of this salt which are unavoidably present in solution of ferric chloride in an organic solvent should be sufficient for the realization of the reaction according to the above-described catalytic mechanism.

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* The oxidation-reduction potential of the system $Fe^{III}Ph/Fe^{II}Ph$, like other analogous hemin systems, is far less positive than the system $Fe^{III}/Fe^{II}$.

** A system which is similar in some aspects to our own was previously proposed [11] for the process of the introduction of iron into the nucleus of mesoporphyrin ester.

*** A number of authors [12] consider that the main reaction which takes place as a result of the reaction of chlorophyll with $FeCl_3$ is the oxidation of the pigment. The conclusions of these authors which are based on experiments carried out in the presence of air, i. e., under conditions in which the main process taking place in these systems is retarded, are not convincing.

# SUMMARY

1. The reaction of chlorophyll with ferric chloride in solutions of ether and acetone leads to the displacement of magnesium from the chlorophyll nucleus and the formation of pheophytin iron-III. The reaction takes place extremely slowly and is characterized by a high temperature coefficient.

2. In acetone solution the reaction takes place via a stage of the formation of an intermediate gray product having a spectrum which is characteristic of dihydroporphin derivatives. The addition of chlorides to a system containing this intermediate product leads to the regeneration of chlorophyll. The conversion of the intermediate gray product to pheophytin iron is an irreversible process.

3. Bivalent iron ions exert a marked catalytic influence on the process of the introduction of iron into the chlorophyll nucleus. Oxygen has an intense retarding effect on the reaction.

4. A system was proposed in which the principal role in the development of the reaction is played by the complex ions $Fe(MgPh)^{+++}$.

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# FURTHER DISCUSSION

## THE PROBLEM OF THE GENERAL DEFINITION OF CHEMISTRY *

### Iu. A. Zhdanov

Our article [1] which led to a number of objections raised by Ia. E. Ekster [2] was published in the Journal of General Chemistry. We can only welcome the desire to clarify the main conceptions of chemical science in a discussion, but Ia. E. Ekster's objections are off the point and his own position seems somewhat contradictory.

We proposed the definition of chemistry as the science of the qualitative changes of bodies, taking place under the influence of changes in their quantitative composition and structure. Any formulation can, of course, be improved and corrected. Ekster supports us, pointing out the inadequacy of the famous definition of Engels (a definition adopted in a whole series of chemical and philosophical works published in this country).

In the final analysis the idea put forward by us amounts to the fact that the definition of chemistry must include the most important feature of chemism: the variation in the structure of substances. In this connection, structure is considered in the Butlerov sense as a stable order of reactions of atoms. The usual definition of chemistry as the science of substances and their changes does not contain this decisive factor and should, therefore, be corrected. This definition reflects the prestructural analytical stage in the development of chemistry.

On the one hand, Ekster objects to our criticism of the definition of chemistry as the science of substances and their changes, considering our proofs to be unconvincing. The fact cannot be escaped, however, that not all the changes of substances are of a chemical nature, in particular, for example, the processes of the transformation of the elements taking place on an enormous scale in the universe.

At the same time Ekster, on the other hand, favors our definition affirming that "the chemical structure of a substance is that inalienable quality which determines its chemical behavior." It is remarkable that having written this, Ekster describes the inclusion of the "inalienable quality" in the definition of chemism as to some extent tautological. In such a case any definition of any concept must be considered tautological, including the definition of chemistry as the science of substances and their changes. Surely it is clear that in the formulation of the general definition of chemistry the basis taken must be that inalienable quality which determines the chemical behavior of substances. Ekster's other objections are not a matter of principle but it is worthwhile, however, to deal with them.

Ekster objects to the term "body" as applied to chemical substances. This term seems reasonably satisfactory to us. Many chemists have employed it successfully, including Berzelius and Butlerov (to mention only his famous definition of the significance of rational formulas: "For each body there will be only one rational formula possible and when the general laws of the relationship between the chemical properties of bodies and their chemical structure becomes known a similar formula will express all these properties").

Ekster further maintains that our proposed definition of chemism excludes from consideration the phenomena of isomerism. This is an obvious misunderstanding. It will be clear to anyone who reads our article carefully that it was precisely the phenomenon of isomerism which was the initial point for the criticism of the analytical definition of the subject of general chemistry. But if we maintain the formal point of view adopted by Ekster it must be pointed out that in the words "composition and structure" the conjunction "and" can have a separating as well as a connecting meaning. When we say that sodium has the capacity to combine with chlorine and bromine, an informed man will hardly think that sodium cannot combined with each of the halogens separately. The word "or"

* Reply to Ia. E. Ekster.

can, of course, be put in brackets at the side of "and" but this does not alter the essence of the matter.

As regards Ekster's remark to the effect that when chemical changes take place, some qualitative indices always undergo a change,    is, of course, correct. The point dealt with in Engels' definition is, however, the number of atoms in molecules which remain  unchanged in isomeric changes.

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* Original Russian pagination.  See C. B. pagination.

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# SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY
## ENCOUNTERED IN SOVIET PERIODICALS

| | |
|---|---|
| FIAN | Phys. Inst. Acad. Sci. USSR. |
| GDI | Water Power Inst. |
| GITI | State Sci.-Tech. Press |
| GITTL | State Tech. and Theor. Lit. Press |
| GONTI | State United Sci.-Tech. Press |
| Gosenergoizdat | State Power Press |
| Goskhimizdat | State Chem. Press |
| GOST | All-Union State Standard |
| GTTI | State Tech. and Theor. Lit. Press |
| IL | Foreign Lit. Press |
| ISN (Izd. Sov. Nauk) | Soviet Science Press |
| Izd. AN SSSR | Acad. Sci. USSR Press |
| Izd. MGU | Moscow State Univ. Press |
| LEIIZhT | Leningrad Power Inst. of Railroad Engineering |
| LET | Leningrad Elec. Engr. School |
| LETI | Leningrad Electrotechnical Inst. |
| LETIIZhT | Leningrad Electrical Engineering Research Inst. of Railroad Engr. |
| Mashgiz | State Sci.-Tech. Press for Machine Construction Lit. |
| MEP | Ministry of Electrical Industry |
| MES | Ministry of Electrical Power Plants |
| MESEP | Ministry of Electrical Power Plants and the Electrical Industry |
| MGU | Moscow State Univ. |
| MKhTI | Moscow Inst. Chem. Tech. |
| MOPI | Moscow Regional Pedagogical Inst. |
| MSP | Ministry of Industrial Construction |
| NII ZVUKSZAPIOI | Scientific Research Inst. of Sound Recording |
| NIKFI | Sci. Inst. of Modern Motion Picture Photography |
| ONTI | United Sci.-Tech. Press |
| OTI | Division of Technical Information |
| OTN | Div. Tech. Sci. |
| Stroiizdat | Construction Press |
| TOE | Association of Power Engineers |
| TsKTI | Central Research Inst. for Boilers and Turbines |
| TsNIEL | Central Scientific Research Elec. Engr. Lab. |
| TsNIEL-MES | Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants |
| TsVTI | Central Office of Economic Information |
| UF | Ural Branch |
| VIESKh | All-Union Inst. of Rural Elec. Power Stations |
| VNIIM | All-Union Scientific Research Inst. of Meteorology |
| VNIIZhDT | All-Union Scientific Research Inst. of Railroad Engineering |
| VTI | All-Union Thermotech. Inst. |
| VZEI | All-Union Power Correspondence Inst. |

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.